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NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2		"Ask CAS" for self-help around the clock
NEWS 3	AUG 09	INSPEC enhanced with 1898-1968 archive
NEWS 4	AUG 28	ADISCTI Reloaded and Enhanced
NEWS 5	AUG 30	CA(SM)/CAplus(SM) Austrian patent law changes
NEWS 6	SEP 11	CA/CAplus enhanced with more pre-1907 records
NEWS 7	SEP 21	CA/CAplus fields enhanced with simultaneous left and right truncation
NEWS 8	SEP 25	CA(SM)/CAplus(SM) display of CA Lexicon enhanced
NEWS 9	SEP 25	CAS REGISTRY(SM) no longer includes Concord 3D coordinates
NEWS 10	SEP 25	CAS REGISTRY(SM) updated with amino acid codes for pyrrolysine
NEWS 11	SEP 28	CEABA-VTB classification code fields reloaded with new classification scheme
NEWS 12	OCT 19	LOGOFF HOLD duration extended to 120 minutes
NEWS 13	OCT 19	E-mail format enhanced
NEWS 14	OCT 23	Option to turn off MARPAT highlighting enhancements available
NEWS 15	OCT 23	CAS Registry Number crossover limit increased to 300,000 in multiple databases
NEWS 16	OCT 23	The Derwent World Patents Index suite of databases on STN has been enhanced and reloaded
NEWS 17	OCT 30	CHEMLIST enhanced with new search and display field
NEWS 18	NOV 03	JAPIO enhanced with IPC 8 features and functionality
NEWS 19	NOV 10	CA/CAplus F-Term thesaurus enhanced
NEWS 20	NOV 10	STN Express with Discover! free maintenance release Version 8.01c now available
NEWS 21	NOV 13	CA/CAplus pre-1967 chemical substance index entries enhanced with preparation role
NEWS 22	NOV 20	CAS Registry Number crossover limit increased to 300,000 in additional databases
NEWS 23	NOV 20	CA/CAplus to MARPAT accession number crossover limit increased to 50,000
NEWS 24	NOV 20	CA/CAplus patent kind codes will be updated
NEWS 25	DEC 01	CAS REGISTRY updated with new ambiguity codes
NEWS 26	DEC 11	CAS REGISTRY chemical nomenclature enhanced

NEWS EXPRESS NOVEMBER 10 CURRENT WINDOWS VERSION IS V8.01c, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 25 SEPTEMBER 2006.

NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS LOGIN	Welcome Banner and News Items
NEWS IPC8	For general information regarding STN implementation of IPC 8
NEWS X25	X.25 communication option no longer available

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FILE 'HOME' ENTERED AT 11:03:55 ON 12 DEC 2006

=> file reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 11:04:11 ON 12 DEC 2006
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STRUCTURE FILE UPDATES: 11 DEC 2006 HIGHEST RN 915185-72-7
DICTIONARY FILE UPDATES: 11 DEC 2006 HIGHEST RN 915185-72-7

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http://www.cas.org/ONLINE/UG/regprops.html

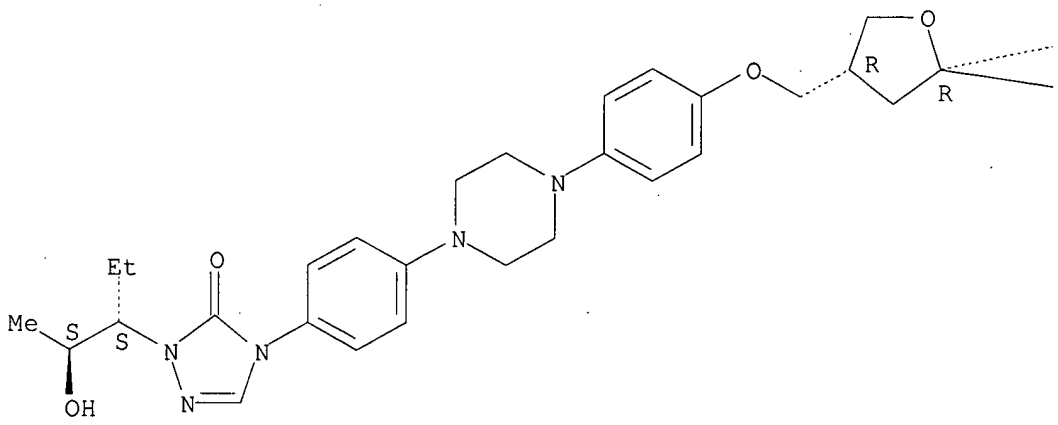
=> s posaconazole/cn
L1 1 POSACONAZOLE/CN

=> d str cn rn

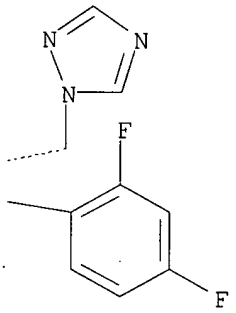
L1 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2006 ACS on STN

Absolute stereochemistry. Rotation (-).

PAGE 1-A



PAGE 1-B



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

CN D-threo-Pentitol, 2,5-anhydro-1,3,4-trideoxy-2-C-(2,4-difluorophenyl)-4-[[4-[4-[4-[1-[(1S,2S)-1-ethyl-2-hydroxypropyl]-1,5-dihydro-5-oxo-4H-1,2,4-triazol-4-yl]phenyl]-1-piperazinyl]phenoxy]methyl]-1-(1H-1,2,4-triazol-1-yl)- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Noxafil
CN Posaconazole
CN Sch 56592
RN 171228-49-2 REGISTRY

=> s posaconazole
L2 1 POSACONAZOLE

=> s SCH56592
L3 0 SCH56592

=> caplus medline biosis embase
CAPLUS IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.

```
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> file caplus medline biosis embase
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                        17.94      18.15

FILE 'CAPLUS' ENTERED AT 11:06:39 ON 12 DEC 2006
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FILE 'BIOSIS' ENTERED AT 11:06:39 ON 12 DEC 2006
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FILE 'EMBASE' ENTERED AT 11:06:39 ON 12 DEC 2006
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=> s posaconazole or 171228-49-2
L4         1875 POSACONAZOLE OR 171228-49-2

=> s SCH56592
L5          126 SCH56592

=> s L4 or L5
L6         1888 L4 OR L5

=> dup rem L6
PROCESSING COMPLETED FOR L6
L7         1201 DUP REM L6 (687 DUPLICATES REMOVED)

=> s L7 and (AY<2003 or PY<2003 or PRY<2003)
'2003' NOT A VALID FIELD CODE
'2003' NOT A VALID FIELD CODE
   2 FILES SEARCHED...
'2003' NOT A VALID FIELD CODE
'2003' NOT A VALID FIELD CODE
'2003' NOT A VALID FIELD CODE
'2003' NOT A VALID FIELD CODE
L8          491 L7 AND (AY<2003 OR PY<2003 OR PRY<2003)

=> s fungal infections
L9        16357 FUNGAL INFECTIONS

=> s L8 and L9
L10         105 L8 AND L9

=> s L10 and (AY<2002 or PY<2002 or PRY<2002)
'2002' NOT A VALID FIELD CODE
'2002' NOT A VALID FIELD CODE
   2 FILES SEARCHED...
'2002' NOT A VALID FIELD CODE
'2002' NOT A VALID FIELD CODE
'2002' NOT A VALID FIELD CODE
'2002' NOT A VALID FIELD CODE
L11          70 L10 AND (AY<2002 OR PY<2002 OR PRY<2002)

=> s neutropenic
L12       18107 NEUTROPENIC

=> s L11 and L12
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```
L13          6 L11 AND L12

=> s plasma concentration
L14     189151 PLASMA CONCENTRATION

=> s L10 and L14
L15          5 L10 AND L14

=> s invasive fungal infection
L16       3125 INVASIVE FUNGAL INFECTION

=> s invasive fungal infections
L17       2396 INVASIVE FUNGAL INFECTIONS

=> s L10 and L16
L18         44 L10 AND L16

=> d L13 1-6 ibib abs

L13  ANSWER 1 OF 6  CAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:         2001:219689  CAPLUS
DOCUMENT NUMBER:          135:40271
TITLE:                    Lipid-based amphotericin B: a review of the last 10
                          years of use
AUTHOR(S):                Hann, I. M.; Prentice, H. G.
CORPORATE SOURCE:         Level II, Department of Haematology, Great Ormond
                          Street Children's Hospital, Camelia Botnar
                          Laboratories, London, WC1N3JH, UK
SOURCE:                   International Journal of Antimicrobial Agents (
                          2001), 17(3), 161-169
                          CODEN: IAAGEA; ISSN: 0924-8579
PUBLISHER:                Elsevier Science Ireland Ltd.
DOCUMENT TYPE:            Journal; General Review
LANGUAGE:                 English
AB   A review with 50 refs.  The last decade has been remarkable for the
     dramatic increase in the prevalence of serious fungal
     infections in patients with hematol. disorders and
     neutropenic cancer patients.  The mortality rate of deep-seated
     infection has been in excess of 90% and there is no doubt that this is one
     of the greatest challenges currently facing hematologists and oncologists.
     The development of the lipid-based drugs - liposomal amphotericin
     (AmBisome®), amphotericin B lipid complex, ABLC (Abelcet®),
     amphotericin B colloidal dispersion, Amphocil (ABCD®), has meant that
     doses of amphotericin B can be safely escalated for the first time while
     the problems of nephrotoxicity, infusion related reactions (including
     chills, rigors, fevers and hypoxia) can be reduced.  These toxicities are
     variably reduced with AmBisome more than Abelcet and more than Amphocil
     and there is little information from randomized trials other than for
     AmBisome.  AmBisome used in the setting of persistent fever and
     neutropenia not responding after 3-4 days of i.v. antibiotics, is associated
     with less breakthrough systemic fungal infections.
     There is also much less need for premedication, including steroids,
     compared with amphotericin B and Abelcet.  The use of intermittent doses
     of AmBisome given prophylactically is now being explored.  A new and
     exciting era of antifungal therapy is opening up with new compds., such as
     itraconazole voriconazole, posaconazole and echinocandins, being
     investigated and for the first time, we also have options for combination
     therapy and prophylaxis.
REFERENCE COUNT:          50    THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS
                                RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13  ANSWER 2 OF 6  EMBASE  COPYRIGHT (c) 2006 Elsevier B.V. All rights
     reserved on STN
ACCESSION NUMBER:    2001274364  EMBASE
```

TITLE: Caspofungin: Pharmacology, safety and therapeutic potential in superficial and invasive fungal infections.
AUTHOR: Groll A.H.; Walsh T.J.
CORPORATE SOURCE: Dr. A.H. Groll, Immunocompromised Host Section, Pediatric Oncology Branch, National Cancer Institute, 10 Center Drive, Bethesda, MD 20892, United States. grolla@mail.nih.gov
SOURCE: Expert Opinion on Investigational Drugs, (2001) Vol. 10, No. 8, pp. 1545-1558. .
Refs: 66
ISSN: 1354-3784 CODEN: EOIDER
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
006 Internal Medicine
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
052 Toxicology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 23 Aug 2001
Last Updated on STN: 23 Aug 2001

AB Invasive fungal infections are important causes of morbidity and mortality in hospitalised patients. Current therapy with amphotericin B and antifungal triazoles has overlapping targets and is limited by toxicity and resistance. The echinocandin lipopeptide caspofungin is the first of a new class of antifungal compounds that inhibit the synthesis of 1,3-β-D-glucan. This homopolysaccharide is a major component of the cell wall of many pathogenic fungi and yet is absent in mammalian cells. It provides osmotic stability and is important for cell growth and cell division. In vitro, caspofungin has broad-spectrum anti-fungal activity against Candida and Aspergillus spp. without cross-resistance to existing agents. The compound exerts prolonged post-antifungal effects and fungicidal activity against Candida species and causes severe damage of Aspergillus fumigatus at the sites of hyphal growth. Animal models have demonstrated efficacy against disseminated candidiasis and disseminated and pulmonary aspergillosis, both in normal and in immunocompromised animals. Caspofungin possesses favourable pharmacokinetic properties and is not metabolised through the CYP450 enzyme system. It showed highly promising antifungal efficacy in Phase II and III clinical trials in immunocompromised patients with oesophageal candidiasis. Caspofungin was effective in patients with invasive aspergillosis intolerant or refractory to standard therapies. Based on its documented antifungal efficacy and an excellent safety profile, caspofungin has been approved recently by the US Food and Drug Administration for the treatment of invasive aspergillosis in patients who are refractory to or intolerant of other therapies (i.e., amphotericin B, lipid formulations of amphotericin B, and/or itraconazole). Phase III clinical trials in patients with candidaemia and in persistently febrile neutropenic patients requiring empirical antifungal therapy are ongoing. This paper reviews the preclinical and clinical pharmacology of caspofungin and its potential role for treatment of invasive and superficial fungal infections in patients.

ACCESSION NUMBER: 2000365900 EMBASE
TITLE: New antifungal agents and preparations.
AUTHOR: De Pauw B.E.
CORPORATE SOURCE: B.E. De Pauw, Department of Hematology, University Hospital Nijmegen, P.O. Box 9101, 6500 HB Nijmegen, Netherlands. b.depauw@hemat.azn.nl

SOURCE: International Journal of Antimicrobial Agents, (2000) Vol. 16, No. 2, pp. 147-150. .
Refs: 11
ISSN: 0924-8579 CODEN: IAAGEA
PUBLISHER IDENT.: S 0924-8579(00)00221-1
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; (Short Survey)
FILE SEGMENT: 025 Hematology
030 Pharmacology
037 Drug Literature Index
004 Microbiology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 16 Nov 2000
Last Updated on STN: 16 Nov 2000

AB In neutropenic patients amphotericin B remains the drug of choice for the treatment of systemic fungal infections . On the basis of a superior efficacy in combination with a lower toxicity, the triazoles have superseded the older azoles. Regularly, amphotericin B and a triazole are used simultaneously without any evidence from clinical trials that such a strategy is safe and efficacious. Liposomal preparation, lipid complex or colloidal dispersion of amphotericin B have been produced successfully to reduce toxicity. However, there is only one small randomised study that hints at the superiority of liposomal amphotericin B over amphotericin B deoxycholate. Promising new agents like candins, sordarins, high dose oral terbinafine, the third generation azoles, and liposomal nystatin are under development. The first phase II study on voriconazole in the treatment of pulmonary aspergillosis has produced encouraging results. The major promise of the new candins lies in the activity against Candida species, including those resistant to the azoles and polyenes, and in a mechanism of action totally different from the established antifungals. Cytokines and colony stimulating factors are theoretically very promising but there are no clinical studies that warrant routine use. Copyright (C) 2000 Elsevier Science B.V.

ACCESSION NUMBER: 1999267506 EMBASE
TITLE: Fungal infections.
AUTHOR: Barnes R.A.
CORPORATE SOURCE: R.A. Barnes, Department of Medical Microbiology, University of Wales, College of Medicine, Cardiff CF4 4XN, United Kingdom
SOURCE: Current Anaesthesia and Critical Care, (1999) Vol. 10, No. 1, pp. 21-26. .
Refs: 29
ISSN: 0953-7112 CODEN: CCCAEI
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 004 Microbiology
017 Public Health, Social Medicine and Epidemiology
024 Anesthesiology
026 Immunology, Serology and Transplantation
029 Clinical Biochemistry
030 Pharmacology
037 Drug Literature Index
039 Pharmacy
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 19 Aug 1999
Last Updated on STN: 19 Aug 1999

AB Systemic fungal infections are a rapidly increasing

problem in critically ill patients and rates have increased significantly in the past 20 years. They represent a major cause of morbidity and mortality in a variety of hospitalized patients including those in neonatal and intensive care units. This trend concerns not only severely compromised hosts such as transplant recipients, neutropenic and HIV-positive patients, but also and non-compromised patients, on intensive care units (ICU) with specific risk factors for infection.

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ACCESSION NUMBER: 1999247543 EMBASE
TITLE: Management of invasive fungal infections in oncological patients.
AUTHOR: Hebart H.; Bokemeyer C.; Loffler J.; Schumacher U.; Kanz L.; Einsele H.
CORPORATE SOURCE: Dr. H. Hebart, Abt. 11, Medizinische Klinik, Eberhard-Karls-Universitat Tubingen, Otfried-Muller-Strasse 10, D-72076 Tubingen, Germany
SOURCE: Onkologie, (1999) Vol. 22, No. 3, pp. 192-197. .
Refs: 37
ISSN: 0378-584X CODEN: ONKOD2
COUNTRY: Germany
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 004 Microbiology
016 Cancer
036 Health Policy, Economics and Management
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English; German
ENTRY DATE: Entered STN: 2 Aug 1999
Last Updated on STN: 2 Aug 1999

AB Invasive fungal infections, especially due to Candida and Aspergillus spp., have become a major cause of infection-related mortality in neutropenic cancer patients. Conventional amphotericin B remains the standard drug for antimycotic therapy, however, new antifungal compounds with broad antifungal activity such as lipid formulations of amphotericin B, new azoles, candins, nikkomycin Z, and pradimicin have been developed and are evaluated in preclinical and clinical studies. In this review the most important antifungal compounds are described, and aspects of disease management in neutropenic and nonneutropenic patients are discussed.

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ACCESSION NUMBER: 1999069771 EMBASE
TITLE: Treatment of fungal infections in neutropenic children.
AUTHOR: Lehrnbecher T.; Groll A.H.; Chanock S.J.
CORPORATE SOURCE: Dr. T. Lehrnbecher, Immunocompromised Host Section, Pediatric Oncology Branch, NCIH, Bldg 10, Room 13N240, 10 Center Drive,, Bethesda, MD 20892, United States
SOURCE: Current Opinion in Pediatrics, (1999) Vol. 11, No. 1, pp. 47-55. .
Refs: 112
ISSN: 1040-8703 CODEN: COPEE
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 004 Microbiology
007 Pediatrics and Pediatric Surgery
016 Cancer
026 Immunology, Serology and Transplantation
030 Pharmacology
037 Drug Literature Index

038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 4 Mar 1999
Last Updated on STN: 4 Mar 1999

AB Fungal infections have emerged as one of the most significant complications of antineoplastic therapy and marrow transplantation in children. Morbidity and mortality associated with fungal infections are high. Recent trends indicate that the incidence and spectrum of fungal infections are increasing, partly because of the increase in the number of children receiving intensive chemotherapy and marrow transplantation, but also because of the successful management of bacterial and viral infections. Though many factors may contribute to risk for developing a fungal infection, prolonged neutropenia is the most important. Until recently, options for antifungal therapy were limited. Advances include less toxic formulations of amphotericin B and an expanding armamentarium of azoles as well as new antifungal compounds. This review addresses the therapeutic options available for treatment of fungal infections in immunocompromised children.

=> d 1-5 L15 ibib abs

L15 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:252195 CAPLUS
DOCUMENT NUMBER: 140:229415
TITLE: Treating fungal infections
INVENTOR(S): Courtney, Rachel; Laughlin, Mark A.
PATENT ASSIGNEE(S): Schering Corporation, USA
SOURCE: U.S. Pat. Appl. Publ., 15 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004058974	A1	20040325	US 2003-667856	20030922 <--
CA 2499897	AA	20040401	CA 2003-2499897	20030919 <--
WO 2004026303	A2	20040401	WO 2003-US29762	20030919 <--
WO 2004026303	A3	20040429		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MA, MD, MG, MK, MN, MX, MZ, NI, NO, NZ, PG, PH, PL, PT, RO, RU, SC, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, US, UZ, VC, VN, YU, ZA, ZM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003282806	A1	20040408	AU 2003-282806	20030919 <--
EP 1542681	A2	20050622	EP 2003-774484	20030919 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003014763	A	20050726	BR 2003-14763	20030919 <--
CN 1688306	A	20051026	CN 2003-822588	20030919 <--
JP 2006503839	T2	20060202	JP 2004-538369	20030919 <--
NO 2005001987	A	20050422	NO 2005-1987	20050422 <--
PRIORITY APPLN. INFO.:			US 2002-412985P P	20020923 <--
			WO 2003-US29762 W	20030919

AB Methods of treating or preventing fungal infections in

humans of 12 yr and older in need of such treating or preventing which comprises orally administering an effective amount of posaconazole in divided doses two to four times a day to produce an arithmetic mean steady state average maximum plasma concn. of posaconazole of at least about 300 ng/mL to at least about 500.

L15 ANSWER 2 OF 5 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 2003:277779 BIOSIS
DOCUMENT NUMBER: PREV200300277779
TITLE: The pharmacokinetic properties of posaconazole in fasted healthy subjects: Basis for clinical dosage recommendations.
AUTHOR(S): Ezzet, F. [Reprint Author]; Wexler, D. [Reprint Author]; Courtney, R. [Reprint Author]; Laughlin, M. [Reprint Author]; Batra, V. [Reprint Author]
CORPORATE SOURCE: Schering-Plough Research Institute, Kenilworth, NJ, USA
SOURCE: Abstracts of the Interscience Conference on Antimicrobial Agents and Chemotherapy, (2002) Vol. 42, pp. 20. print.
Meeting Info.: 42nd Interscience Conference on Antimicrobial Agents and Chemotherapy. San Diego, CA, USA. September 27-30, 2002. American Society for Microbiology.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 11 Jun 2003
Last Updated on STN: 11 Jun 2003

AB Background: Posaconazole (POS) is a potent broad-spectrum antifungal agent currently in clinical development for the treatment of invasive fungal infections. The objective of this study was to determine the pharmacokinetics (PK) of POS following the administration of a total POS dose of 800 mg under three different dosage regimens in healthy, fasted volunteers. Methods: Eighteen fasted, healthy volunteers participated in this Phase I, randomized, open-label, 3-way crossover study. Subjects recevied one of three regimens: A single 800 mg dose (Regimen A), two 400 mg doses separated by 12 hr (Regimen B), or four 200 mg doses separated by 6 hr (Regimen C). Plasma POS concentrations were determined from 0-48 hr post-initial dose using a validated HPLC assay. A one compartment oral model with a 1st order rate of absorption and 1st order rate of elimination was fit to the plasma concentration-time data. Differences in exposure were investigated by allowing the bioavailability fraction (F) to vary between regimens. Results: The absorption rate constant was estimated to be 0.2 hr-1, giving an estimated absorption half-life of 3.5 hr. The elimination rate constant was estimated to be 0.045 hr-1, giving an estaimated termination half-life of 15 hr. F was estimated to be significantly different between regimens (p-value>0.0001). Compared to Regimen A, F for Regimens B and C were estimated to be 1.98 (SE=0.35) and 3.2 (0.7), i.e., an increase in bioavailability of 98% and 220%, respectively. Assuming that the model is predictive upon multiple dosing, steady-state projections would yield AUC (0-24 hr) values of 3900, 7700, and 12400 ng.hr/mL and average concentrations of 162, 320, and 517 ng/mL for Regimens A, B, and C, respectively. Conclusions: Exposure is significantly increased with splitting the 800 mg dose into either 2 (i.e., 2X400 mg) or 4 (i.e., 4X200 mg) doses in fasted, healthy subjects. To enhance exposure under fasted conditions, a split dose regimen is recommended.

L15 ANSWER 3 OF 5 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 2002:499319 BIOSIS
DOCUMENT NUMBER: PREV200200499319
TITLE: Potential for a drug interaction between Posaconazole and Rifabutin.
AUTHOR(S): Courtney, R. D. [Reprint author]; Statkevich, P. [Reprint

author]; Laughlin, M. [Reprint author]; Radwanski, E. [Reprint author]; Lim, J. [Reprint author]; Clement, R. P. [Reprint author]; Batra, V. K. [Reprint author]
CORPORATE SOURCE: Schering-Plough Research Institute, Kenilworth, NJ, USA
SOURCE: Abstracts of the Interscience Conference on Antimicrobial Agents and Chemotherapy, (2001) Vol. 41, pp. 4-5. print.
Meeting Info.: 41st Annual Meeting of the Interscience Conference on Antimicrobial Agents and Chemotherapy. Chicago, Illinois, USA. September 22-25, 2001.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)
LANGUAGE: English
ENTRY DATE: Entered STN: 25 Sep 2002
Last Updated on STN: 25 Sep 2002

AB Background: Posaconazole (POZ) is a broad-spectrum triazole antifungal agent developed to treat a wide variety of invasive fungal infections. POZ inhibits CYP3A4 metabolism, whereas, Rifabutin (RB) is an inducer of CYP3A4. Methods: A non-randomized, open-label, parallel-group, multiple-dose study was conducted to assess the potential for a drug interaction between RB and POZ. Healthy adult male volunteers (n=24) received either of the following two treatments: POZ (200 mg QD) on Days 1 to 10, or RB (300 mg QD) on Day -7 to Day 10 co-administered with POZ (200 mg QD) on Days 1 to 10. Blood samples were collected on Days -1 (RB) and 10 (RB and POZ) for pharmacokinetic (PK) evaluation. Plasma POZ and RB concentration-time data were analyzed by model-independent methods and the PK parameters were statistically evaluated using ANOVA. Changes in the area under the curve within a dosing interval (AUC(tau)) and maximum plasma concentration (Cmax) were evaluated for RB and POZ following co-administration. Results: The mean PK parameters for POZ and RB at steady-state. Conclusion: Clearance of POZ increased 2-fold in the presence of RB while Cmax and AUC(tau) values were reduced by 57 and 51%, respectively. Plasma RB Cmax and AUC(tau) values after co-administration with POZ increased by 31 and 72%, respectively. Therefore, at this time we cannot recommend co-administration of POZ with RB.

L15 ANSWER 4 OF 5 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 2002:499318 BIOSIS
DOCUMENT NUMBER: PREV200200499318
TITLE: Potential for a drug interaction between Posaconazole and Phenytoin.
AUTHOR(S): Courtney, R. D. [Reprint author]; Statkevich, P. [Reprint author]; Laughlin, M. [Reprint author]; Pai, S. [Reprint author]; Lim, J. [Reprint author]; Clement, R. P. [Reprint author]; Batra, V. K. [Reprint author]
CORPORATE SOURCE: Schering-Plough Research Institute, Kenilworth, NJ, USA
SOURCE: Abstracts of the Interscience Conference on Antimicrobial Agents and Chemotherapy, (2001) Vol. 41, pp. 4. print.
Meeting Info.: 41st Annual Meeting of the Interscience Conference on Antimicrobial Agents and Chemotherapy. Chicago, Illinois, USA. September 22-25, 2001.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)
LANGUAGE: English
ENTRY DATE: Entered STN: 25 Sep 2002
Last Updated on STN: 25 Sep 2002

AB Background: Posaconazole (POZ) is a broad-spectrum triazole antifungal agent developed to treat a wide variety of invasive fungal infections. POZ inhibits CYP3A4 metabolism, whereas, Phenytoin (PH) is an inducer of CYP3A4 metabolism. Methods: This

randomized, open-label, parallel-group, multiple-dose study with POZ and PH was conducted in healthy male and female adult volunteers (n=36) to assess the potential for a drug interaction between PH and POZ. Each subject was randomized to receive one of the following three treatments: Treatment A: POZ (200 mg QD) for 10 days, Treatment B: PH (200 mg QD) for 10 Days, and Treatment C: POZ (200 mg QD) and PH (200 mg QD) for 10 days. Blood samples were collected on Days 1 and 10 for pharmacokinetic (PK) evaluation of POZ and PH. Plasma data were analyzed by model-independent methods, and PK parameters were evaluated using ANOVA to assess changes in the area under the curve over 24 hr (AUC(0-24hr)), maximum plasma concentration (Cmax) and accumulation ratio (R) between Days 1 and 10 for both POZ and PH. Results: Cmax and AUC(0-24hr) values of POZ on Day 10 when administered alone were approximately 2-fold higher than those on Day 1 (R apprx2); the steady state clearance (CL/F) on Day 10 was 30.3L/hr. In the presence of PH, however, the CL/F increased by apprx90% and the Cmax and AUC(0-24hr) values of POZ on Day 10 were similar to those on Day 1 (R apprx1). Within the limits of variability (%CV ranging from 22-77%), PH Cmax and AUC(0-24 hr) values showed no statistically significant differences ($p>0.05$) following single and multiple dose administration of PH in the presence or absence of POZ. Conclusion: The large variability in the Cmax and AUC(0-24hr) values was due to some individuals with clinically significant increases in exposure of PH in the presence of POZ. Therefore, at this time we cannot recommend co-administration of POZ with PH.

L15 ANSWER 5 OF 5 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 2002:499317 BIOSIS
DOCUMENT NUMBER: PREV200200499317
TITLE: Effect of Posaconazole on the pharmacokinetics of Cyclosporine.
AUTHOR(S): Courtney, R. D. [Reprint author]; Statkevich, P. [Reprint author]; Laughlin, M. [Reprint author]; Lim, J. [Reprint author]; Clement, R. P. [Reprint author]; Batra, V. K. [Reprint author]
CORPORATE SOURCE: Schering-Plough Research Institute, Kenilworth, NJ, USA
SOURCE: Abstracts of the Interscience Conference on Antimicrobial Agents and Chemotherapy, (2001) Vol. 41, pp. 4. print.
Meeting Info.: 41st Annual Meeting of the Interscience Conference on Antimicrobial Agents and Chemotherapy. Chicago, Illinois, USA. September 22-25, 2001.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)
LANGUAGE: English
ENTRY DATE: Entered STN: 25 Sep 2002
Last Updated on STN: 25 Sep 2002

AB Background: Posaconazole (POZ) is a broad-spectrum triazole antifungal agent developed to treat a wide variety of invasive fungal infections. Cyclosporine (CS) is metabolized by the CYP3A4 metabolic pathway, which is inhibited by POZ. Methods: This open-label, multiple-dose study was conducted to assess the potential for a drug interaction between CS and POZ. Male and female adult heart transplant patients (n=4) maintained on CS upon entering the study, received 200 mg POZ (QD) for 10 days. Blood samples were collected on Days 1 (CS only) and 10 (CS+POZ) for pharmacokinetic analysis. CS safety monitoring was conducted on Days 2, 3, 5, 8, 21 and 28 prior to the morning CS dose. If CS concentrations were elevated dose adjustments were made. POZ and CS concentration-time data were analyzed using model-independent methods. CS maximum plasma concentration (Cmax) and area under the curve values within a dosing interval (AUC(tau)) were dose normalized (DN). Results: Three of the four patients that completed the study required adjustment of their CS dose (14.3-28.6% reduction). The individual steady-state CS clearance

values were 16-33% lower on Day 10 vs. Day 1. The DN-Cmax and DN-AUC(tau) values of CS on Day 10 in the presence and absence of POZ differed by only 4.2%. The dosage adjustments were considered low, but indicated that CS concentrations increased when co-administered with POZ. Conclusion: Concomitant administration of CS and POZ led to a 0-29% reduction of CS doses in heart transplant patients. POZ was safe and well tolerated but monitoring of patient CS concentrations for dosage adjustments is recommended when CS is co-administered with POZ.

=> d 1-44 ibib abs L18

L18 ANSWER 1 OF 44 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:900211 CAPLUS
DOCUMENT NUMBER: 139:190315
TITLE: Laboratory evaluation of new antifungal agents against rare and refractory mycoses
AUTHOR(S): Sutton, Deanna A.
CORPORATE SOURCE: Dept. of Pathology, Fungus Testing Laboratory, University of Texas Health Science Center at San Antonio, San Antonio, TX, 78229-3900, USA
SOURCE: Current Opinion in Infectious Diseases (2002), 15(6), 575-582
CODEN: COIDE5; ISSN: 0951-7375
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. An increase in refractory invasive fungal infections in the setting of marrow/solid organ transplantation and other immune-compromising clin. entities has provided the impetus for the development of new, more efficacious/less toxic antifungal agents. This review (1) examines currently available laboratory methods for the in-vitro evaluation of these new agents against both yeasts and filamentous fungi; (2) provides a summary of the most attractive investigational agents currently undergoing clin. trials/development; and (3) outlines the major refractory mycoses in contemporary medicine. Fluconazole-resistant Candida spp., Trichosporon spp., zygomycetous genera, the endemic mycoses, Scedosporium, Aspergillus, and Fusarium spp., and an ever-expanding list of lesser-known hyaline and phaeoid genera inciting invasive fungal infections comprise the bulk of refractory mycoses in the immune-compromised host. In-vitro data generated from reference-based antifungal susceptibility testing methods indicate an increased armamentarium of potentially efficacious agents against most of these mycoses. The newly approved antifungal agents caspofungin and voriconazole, used either as monotherapy or in combination regimens, have a significantly improved spectrum of activity over previously available therapeutic options. Correlation of clin. outcomes with investigational agents demonstrating in-vivo/in-vitro activity will provide critical information needed for the development of clin. significant min. inhibitory concentration interpretative breakpoints.
REFERENCE COUNT: 91 THERE ARE 91 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 2 OF 44 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:828005 CAPLUS
DOCUMENT NUMBER: 135:312927
TITLE: New antifungal agents currently under clinical development
AUTHOR(S): Yamaguchi, Hideyo
CORPORATE SOURCE: Teikyo University Institute of Medical Mycology, Hachioji, Tokyo, 192-0395, Japan
SOURCE: Nippon Kagaku Ryoho Gakkai Zasshi (2001), 49(9), 535-545

CODEN: NKRZE5; ISSN: 1340-7007
PUBLISHER: Nippon Kagaku Ryoho Gakkai
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese

AB A review with refs. Currently available antifungal agents for the treatment of invasive fungal infections are limited in number and usefulness. Thus, the development of novel antifungal agents, including new formulations of approved agents, with advantages over and/or complimentary to existing agents is urgently needed. Antifungal agents presently at different clin. development stages in the United States, Europe, and Japan include: (i) various lipid formulations of polyenes (particularly amphotericin B); (ii) hydroxypropyl-β-cyclodextrin formulations of itraconazole; (iii) new generation triazoles; and (iv) candins. Novel delivery systems utilized for the new formulations of polyenes and intraconazole substantially modulate the pharmacokinetics of the existing compds., and may also be useful in enhancing the delivery of antifungal agents to infection sites. The new generation of triazoles, including voriconazole, posaconazole, and ravuconazole, presently at advanced stages of clin. development exhibit and increased activity and expanded spectrum compared with fluconazole and generally demonstrate good pharmacol. properties and low toxicity. Candins represent a novel class of antifungal agents that act by inhibiting the synthesis of (1→3)-β-glucan synthase, a key enzyme in fungal cell wall biosynthesis. Three compds. in this class, viz., VER-002, MK-0991, and FK 463, are fungicidal and active against various fungal pathogens and Pneumocystis carinii without cross-resistance to azoles and show excellent pharmacokinetics and low toxicity. These promising new agents are expected to become available in the near future and should constitute effective new options for the management of a variety of invasive fungal infections.

L18 ANSWER 3 OF 44 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:121724 CAPLUS
DOCUMENT NUMBER: 135:116322
TITLE: New targets and delivery systems for antifungal therapy
AUTHOR(S): Walsh, T. J.; Viviani, M. -A.; Arathoon, E.; Chiou, C.; Ghannoum, M.; Groll, A. H.; Odds, F. C.
CORPORATE SOURCE: Immunocompromised Host Section, Pediatric Oncology Branch, National Cancer Institute, Bethesda, MD, 20892, USA
SOURCE: ✓ Medical Mycology (2000), 38(Suppl. 1), 335-347
CODEN: MEMYFR; ISSN: 1369-3786
PUBLISHER: BIOS Scientific Publishers Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review, with 83 refs. Development of new approaches for treatment of invasive fungal infections encompasses new delivery systems for approved and investigational compds., as well as exploiting the cell membrane, cell wall and virulence factors as putative antifungal targets. Novel delivery systems consisting of cyclodextrins, cochleates, nanoparticles/nanospheres and long circulating ("stealth") liposomes, substantially modulate the pharmacokinetics of existing compds., and may also be useful to enhance the delivery of antifungal agents to sites of infection. Further insights into the structure-activity relationship of the antifungal triazoles that target the biosynthesis of ergosterol in the fungal cell membrane have led to the development of highly potent broad spectrum agents, including posaconazole, ravuconazole and voriconazole. Similarly, a novel generation of cell-wall active semisynthetic echinocandin 1,3 β-glucan inhibitors (caspofungin, FK463, and VER-002) has entered clin. development. These agents have potent and broad-spectrum activity against Candida spp, and potentially useful activity against Aspergillus

spp. and Pneumocystis carinii. The ongoing convergence of the fields of mol. pathogenesis, antifungal pharmacol. and vaccine development will afford the opportunity to develop novel targets to complement the existing antifungal armamentarium.

REFERENCE COUNT: 83 THERE ARE 83 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 4 OF 44 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:569786 CAPLUS
DOCUMENT NUMBER: 133:246681
TITLE: New investigational antifungal agents for treating invasive fungal infections
AUTHOR(S): Hossain, Mohammad A.; Ghannoum, Mahmoud A.
CORPORATE SOURCE: Center for Medical Mycology, Department of Dermatology, Case Western Reserve University and University Hospitals of Cleveland, Cleveland, OH, 44106-5028, USA
SOURCE: Expert Opinion on Investigational Drugs (2000), 9(8), 1797-1813
CODEN: EOIDER; ISSN: 1354-3784
PUBLISHER: Ashley Publications Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 118 refs. Systemic fungal infections have been recognized as a major cause of morbidity and mortality during the last two decades. There are only a few therapeutic options for these infections. Severe toxicity, such as impairment of renal function, limits the use of amphotericin B. Flucytosine is associated with side effects and drug resistance. Fluconazole and itraconazole are safer, though emergence of resistance and innate resistance in some fungal pathogens is a concern in their use. Therefore, there is a need for developing novel drugs and/or treatment strategies to combat these infections. In recent years, increased efforts by the pharmaceutical industry and academia have led to the discovery of new re-engineered or reconsidered antifungal agents that are more efficacious, safer and have a broad spectrum of activity. Lipid formulations of polyene antifungal agents, amphotericin B and nystatin, have the advantage of improved therapeutic index. Activity against resistant fungi, high bioavailability, safety and longer half-life are the properties that encourage development of the newer triazoles (e.g., voriconazole, ravuconazole and posaconazole). Echinocandin-like lipopeptide antibiotics are among the antifungal agents with a novel mode of action. In addition to these lead investigational compds., development of newer antifungal agents is underway.

REFERENCE COUNT: 118 THERE ARE 118 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 5 OF 44 MEDLINE on STN
ACCESSION NUMBER: 2005342419 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15995924
TITLE: Clinical microbiology and infectious diseases. Management of fungal infections.
AUTHOR: Arikan S
CORPORATE SOURCE: Hacettepe University School of Medicine, Infectious Diseases and Clinical Microbiology Department, School of Medicine, Ankara 06100, Turkey..
sarikan@rorqual.cc.metu.edu.tr
SOURCE: IDrugs : the investigational drugs journal, (2001 Jul) Vol. 4, No. 7, pp. 746-9.
Journal code: 100883655. ISSN: 1369-7056.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: NONMEDLINE; PUBMED-NOT-MEDLINE

ENTRY MONTH: 200507
ENTRY DATE: Entered STN: 6 Jul 2005
Last Updated on STN: 14 Jul 2005
Entered Medline: 13 Jul 2005

AB Invasive fungal infections are a major cause of morbidity and mortality in immunocompromised patients. Despite remarkable progress in mycology, many uncertainties and difficulties remain. Invasive fungal infections are difficult to diagnose. Noninvasive, rapid diagnostic tools, such as the detection of Aspergillus galactomannan antigen in serum or of fungal nucleic acids by molecular methods are promising, but are still under investigation. The other difficulty in diagnosis is the lack of standard, consistent criteria. Very recently, diagnostic criteria based on host factors, as well as clinical features and microbiological results, have been proposed. Treatment of invasive fungal infections is also problematic. The development of novel antifungal compounds constitutes a major advance in antifungal therapy. These include novel azoles such as voriconazole (Pfizer), posaconazole (Schering- Plough), and ravuconazole (Eisai/Bristol-Myers Squibb), and novel echinocandins such as caspofungin (Merck), anidulafungin (Eli Lilly), and micafungin (Fujisawa Pharmaceutical). These agents appear more efficacious and less toxic than currently available antifungal drugs. However, immune status of the host remains one of the major determinants of clinical outcome. This property limits the efficiency of in vitro antifungal susceptibility tests in predicting in vivo outcome. Using immune system modifiers such as cytokines in combination with antifungal agents is beneficial in the improvement of immune status, and thus clinical outcome.

L18 ANSWER 6 OF 44 MEDLINE on STN
ACCESSION NUMBER: 2002735077 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12497718
TITLE: [Antifungal treatments].
Les traitements antifongiques.
AUTHOR: Granier Francoise
CORPORATE SOURCE: Service de maladies infectieuses et tropicales CH F. Quesnay, 78200 Mantes-la-Jolie.. f.granier@ch-mantes-la-jolie.rss.fr
SOURCE: Presse medicale (Paris, France : 1983), (2002 Nov 30) Vol. 31, No. 38, pp. 1785-91. Ref: 29
Journal code: 8302490. ISSN: 0755-4982.
PUB. COUNTRY: France
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: French
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200301
ENTRY DATE: Entered STN: 27 Dec 2002
Last Updated on STN: 8 Jan 2003
Entered Medline: 7 Jan 2003

AB THE SITUATION: Invasive fungal infections are increasing and are associated with high rates of morbidity and mortality. The recent emergence of new molecules and antifungal classes raises the hope of new therapeutic perspectives. SECOND GENERATION TRIAZOLES: Voriconazole, ravuconazole and posaconazole have a broader spectrum than the first generation, including notably Aspergillus species and Candida species, resistant to fluconazole. ECHINOCANDINES: Caspofongine and micafongine belong to a new family of antifungals: echinocandines. With a different mechanism of action, they affect the fungal wall. PRESENT RESEARCHES: Are oriented towards the exploration of prophylaxis in patients at risk and, in particular, towards antifungal combinations. However, regarding the latter, in vitro studies and experiments in animals are rare and sometimes contradicting, and clinical trials are almost inexistent.

L18 ANSWER 7 OF 44 MEDLINE on STN
ACCESSION NUMBER: 2002327782 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12070828
TITLE: Invasive Aspergillus infections in hematologic malignancy patients.
AUTHOR: Perea Sofia; Patterson Thomas F
CORPORATE SOURCE: Department of Medicine, Division of Infectious Diseases, The University of Texas Health Science Center at San Antonio, 78229-3900, USA.
SOURCE: Seminars in respiratory infections, (2002 Jun) Vol. 17, No. 2, pp. 99-105. Ref: 64
Journal code: 8700961. ISSN: 0882-0546.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200208
ENTRY DATE: Entered STN: 19 Jun 2002
Last Updated on STN: 10 Aug 2002
Entered Medline: 9 Aug 2002

AB The incidence of invasive Aspergillus (IA) infections in patients with hematologic malignancies continues to increase. The most common species include Aspergillus fumigatus (approximately 90% of cases), A. flavus, A. niger, A. terreus, and A. nidulans. Most infections involve the pulmonary parenchyma, though systemic dissemination of the fungus from a primary pulmonary focus or the paranasal sinuses after hyphal invasion into blood vessels is frequent. Early diagnosis and initiation of appropriate antifungal therapy has been shown to improve the prognosis of patients afflicted with this condition. The definitive diagnosis of IA is based on showing the hyphal invasion in tissue specimens together with a positive culture for Aspergillus species from the same specimen. The detection of circulating fungal antigens and DNA seems to be a promising, rapid, and sensitive diagnostic tool for early diagnosis of aspergillosis. The current antifungals available for the treatment of IA include amphotericin B deoxycholate and lipid formulations, itraconazole and caspofungin acetate. New investigational antifungal drugs include the triazoles voriconazole, posaconazole and ravuconazole, liposomal nystatin, and 2 echinocandin derivatives (anidulafungin [VER-002] and micafungin [FK463]). Preventive measures include reduction of environmental exposure of patients from sources of infection and anti-fungal prophylaxis. Specialized air-handling systems capable of excluding Aspergillus spores, such as high-efficiency particulate air (HEPA) filtration with or without laminar air flow ventilation has proven to be very efficacious. Targeted antifungal prophylaxis for hematologic patients who are at high risk for developing invasive fungal infections is not currently standardized.

L18 ANSWER 8 OF 44 MEDLINE on STN
ACCESSION NUMBER: 2001080943 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11155734
TITLE: [Invasive fungal infections. Epidemiology and new therapies].
Les infections fongiques invasives. Epidemiologie et nouvelles therapeutiques.
AUTHOR: Granier F
CORPORATE SOURCE: Service de Medecine interne et Maladies infectieuse, CH F. Quesnay, boulevard Sully, F 78200 Mantesla-Jolie.. ftremo@hotmail.com
SOURCE: Presse medicale (Paris, France : 1983), (2000 Dec 2) Vol. 29, No. 37, pp. 2051-6. Ref: 25
Journal code: 8302490. ISSN: 0755-4982.

PUB. COUNTRY: France
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: French
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200101
ENTRY DATE: Entered STN: 22 Mar 2001
Last Updated on STN: 22 Mar 2001
Entered Medline: 11 Jan 2001

AB RISING INCIDENCE: In the past two decades, systemic fungal infections, essentially invasive candidiasis, but also invasive aspergillosis, has increased substantially. Despite the currently available antifungal drugs, amphotericin B (AmB), azole compounds (fluconazole or FLU, itraconazole or ITR), these infections are associated with significant morbidity and mortality. AmB remains the drug of choice for treatment of most fungal diseases because of its broad spectrum and potent fungicidal activity, but significant side effects limit its clinical utility. The azole antifungal agents are easier to take, less toxic than AmB, but their use is limited by multiazole-resistant strains. NEW ANTIFUNGAL AGENTS: Lipid formulations have recently attracted much attention due to a significantly lower toxicity: this concerns lipid formulations of AmB and perhaps nystatin in the future. New triazoles (voriconazole, ravuconazole, posaconazole) have shown a wide spectrum of action including against azole-resistant isolates. A new class of antifungal agents, lipopeptides (MK-0991, LY303366, FK463), with an original mechanism of action are being developed. These new compounds are reported to possess a large fungicidal activity against most isolates including AmB and azole-resistant strains.

L18 ANSWER 9 OF 44 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 2003:402796 BIOSIS
DOCUMENT NUMBER: PREV200300402796
TITLE: Prevention and treatment of invasive fungal infections in patients with cancer: The emerging roles of new triazoles and echinocandins.
AUTHOR(S): Walsh, Thomas J. [Reprint Author]
CORPORATE SOURCE: National Cancer Institute, Bethesda, MD, USA
SOURCE: Abstracts of the Interscience Conference on Antimicrobial Agents and Chemotherapy, (2002) Vol. 42, pp. 457. print.
Meeting Info.: 42nd Interscience Conference on Antimicrobial Agents and Chemotherapy. San Diego, CA, USA. September 27-30, 2002. American Society for Microbiology.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 3 Sep 2003
Last Updated on STN: 3 Sep 2003

AB Invasive fungal infections have emerged as important causes of morbidity and mortality in immunocompromised patients with cancer, particularly those persistent neutropenia, BMT, or other severe immunodeficiency. Once developed, these infections may carry an ominous prognosis. The introduction of second generation triazoles and echinocandins provides new opportunities for therapeutic intervention and prevention of these infections. The second-generation triazoles include voriconazole, posaconazole, and ravuconazole. These compounds, which were developed through in vitro screening against Aspergillus spp., have low MICs, a broad antifungal spectrum against yeasts, and filamentous fungi beyond Aspergillus spp., parenteral and oral formulations, a favorable safety profile, and plasma half-life permitting once or twice daily dosing. The echinocandins are cyclic hexapeptides with modified N-acyl side chains that permit expanded antifungal spectrum, which includes Candida spp., Aspergillus spp., Pneumocystis carinii, but not

Cryptococcus neoformans. As relatively large molecules, the echinocandins have minimal oral bioavailability and are provided only as parenteral solutions. The recent results of clinical trials with these compounds indicate that they will likely change the patterns of future practice in the treatment and prevention of infections in patients with cancer.

L18 ANSWER 10 OF 44 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 2003:328301 BIOSIS
DOCUMENT NUMBER: PREV200300328301
TITLE: Combination treatment of posaconazole (POS) and amphotericin B (AmB) against Candida albicans in a mouse systemic infection model.
AUTHOR(S): Cacciapuoti, A. F. [Reprint Author]; Gurnani, M. [Reprint Author]; Halpern, J. [Reprint Author]; Gheyas, F. [Reprint Author]; Hare, R. [Reprint Author]; Loebenberg, D. [Reprint Author]
CORPORATE SOURCE: Schering-Plough Research Institute, Kenilworth, NJ, USA
SOURCE: Abstracts of the Interscience Conference on Antimicrobial Agents and Chemotherapy, (2002) Vol. 42, pp. 415. print.
Meeting Info.: 42nd Interscience Conference on Antimicrobial Agents and Chemotherapy. San Diego, CA, USA. September 27-30, 2002. American Society for Microbiology.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 16 Jul 2003
Last Updated on STN: 16 Jul 2003

AB Background: POS (SCH 56592) is a triazole, currently in Phase II clinical trials, with broad-spectrum activity against fungi. Since AmB is considered the gold standard for antifungal treatment of severe invasive fungal infections, we wanted to determine that the addition of POS treatment would have no deleterious effect. Methods: Normal mice were infected intravenously with 5X106 or 1X107 CFU/mouse of C. albicans C43 (Fluconazole (FLZ)-susceptible), C210 (FLZ-susceptible-dose-dependent), C284 or C335 (FLZ-resistant). Treatment of groups of 10 mice with POS (oral), AmB (intraperitoneal) or concomitant POS+AmB (POS dosed immediately prior to AmB) began 4 h postinfection and continued once daily for 4 days. POS and AmB were tested at 4 dose levels alone or in all possible combinations in a checkerboard fashion. Controls were dosed with sterile water for injection. Survival was observed for 10 days. Each strain was tested twice and the data pooled for statistical analysis. Wilcoxon tests were performed on survival curves (Kaplan-Meier) to compare combinations to the component monotherapies. Results: Summarizing the pooled results for all 4 C. albicans strains, the survival curves of mice treated with POS+AmB combinations were either similar to ($p>0.05$), or more efficacious ($p<0.05$) than, either component monotherapy in 117 comparisons. Only 1 was less efficacious ($p<0.05$) and 10 were indeterminable. Conclusion: Treatment with concomitant combinations of POS+AmB had no negative effects on the survival of mice compared to that of the individual components.

L18 ANSWER 11 OF 44 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 2003:277822 BIOSIS
DOCUMENT NUMBER: PREV200300277822
TITLE: Effect of cimetidine on the pharmacokinetics of Posaconazole in healthy volunteers.
AUTHOR(S): Courtney, R. [Reprint Author]; Wexler, D. [Reprint Author]; Statkevich, P. [Reprint Author]; Lim, J. [Reprint Author]; Batra, V. [Reprint Author]; Laughlin, M. [Reprint Author]
CORPORATE SOURCE: Schering-Plough Research Institute, Kenilworth, NJ, USA
SOURCE: Abstracts of the Interscience Conference on Antimicrobial

Agents and Chemotherapy, (2002) Vol. 42, pp. 29.
print.
Meeting Info.: 42nd Interscience Conference on Antimicrobial Agents and Chemotherapy. San Diego, CA, USA. September 27-30, 2002. American Society for Microbiology.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 11 Jun 2003
Last Updated on STN: 11 Jun 2003

AB Background: Posaconazole (POS) is a potent broad spectrum antifungal agent currently in clinical development for the treatment of invasive fungal infections. POS in primarily excreted as parent drug with minor glucuronide metabolites into the urine. Cytochrome P450 enzymes do not metabolize POS. The primary objective of this study was to evaluate the effect of cimetidine on the pharmacokinetics (PK) of POS. Methods: Twelve healthy subjects completed this randomized, open-label, 2-way crossover, multiple-dose interaction study between POS and cimetidine. The subjects received POS (200 mg) tablets once a day with food for 10 consecutive days in the presence and absence of cimetidine (400 mg every 12 hr). The treatments were separated by a 7-day washout. On Days 1 and 10, blood samples were collected from 0 to 120 hr and analyzed for POS using a validated high performance liquid chromatographic assay. The PK of POS were determined using model independent methods and statistically analyzed using ANOVA. Results: Concomitant administration of POS and cimetidine decreased the Cmax and AUC(tau) of POS by apprx40% compared to the administration of POS alone. The relative oral bioavailability estimate for both Cmax and AUC(tau) was 61%, and the 90% confidence intervals were 54-69% and 53-70%, respectively. POS was orally bioavailable with the mean Cmax reached by apprx7.0 hr postdose. The Tmax and terminal phase t1/2 of POS (apprx35 hr) were independent of treatment. Conclusions: 1) POS was safe and well tolerated following multiple dose administration. 2) There was an interaction of cimetidine with POS based on Cmax and AUC(tau), with cimetidine decreasing POS exposure by apprx40%.

L18 ANSWER 12 OF 44 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 2003:277821 BIOSIS
DOCUMENT NUMBER: PREV200300277821
TITLE: Effect of food and antacid on the pharmacokinetics of Posaconazole in healthy volunteers.
AUTHOR(S): Courtney, R. [Reprint Author]; Statkevich, P. [Reprint Author]; Lim, J. [Reprint Author]; Laughlin, M. [Reprint Author]; Batra, V. [Reprint Author]
CORPORATE SOURCE: Schering-Plough Research Institute, Kenilworth, NJ, USA
SOURCE: Abstracts of the Interscience Conference on Antimicrobial Agents and Chemotherapy, (2002) Vol. 42, pp. 29.
print.
Meeting Info.: 42nd Interscience Conference on Antimicrobial Agents and Chemotherapy. San Diego, CA, USA. September 27-30, 2002. American Society for Microbiology.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 11 Jun 2003
Last Updated on STN: 11 Jun 2003

AB Background: Posaconazole (POS) is a potent broad-spectrum antifungal agent currently in clinical development for the treatment of invasive fungal infections. The objectives of this study were to evaluate the potential for a food effect and a pH-dependent pharmacokinetic interaction between POS and an antacid (MylantaTM). Methods: Twelve healthy male volunteers completed this randomized, 4 period crossover, single-dose interaction study between POS

and the antacid under fed and fasted conditions. Subjects received POS (200 mg tabelts every 24 hr), following Treatment A: a 10-hr fast. Treatment B: 20 mL MylantaTM and a 10-hr fast. Treatment C: 20 mL MylantaTM and a standardized high-fat breakfast. Treatment D: a standardized high-fat breakfast. Each treatment was separated by a 7-day washout. Blood samples were collected from 0 to 72 hr and analyzed using model independent methods and statistically analyzed using ANOVA. Results: In the fasted state, based on AUC(tf) ratios, antacid increased the relative oral bioavailability 15% (confidence interval (CI) range of 92-143%); whereas in the fed state antacid decreased the relative bioavailability 12% (CI range 71-110%). Food increased the relative oral bioavilability (AUC(tf)) of POS 400%, with a corresponding 90% CI range of 322-497%. The extent of POS administration was affected by food, with both an increase of Cmax (93 vs. 366 ng/mL) and AUC(tf) (2718 vs. 10220 ng.hr/mL) observed. POS was orally bioavailable with a median Tmax of 8.7 hr, which was independent of treatment. Conclusions: 1) The effect of antacid on POS AUC(tf) in either the fed or fasted state was small, taking into consideration the variability (CV range 29-45%), and is not considered clinically significant. 2) In the presence of a high-fat meal the bioavailaibity of POS increased 4 fold. Therefore, it is recommended that POS be administered whenever possible with a meal or nutritional suppliment, preferably with a high-fat content, to maximize absorption.

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ACCESSION NUMBER: 2003:277779 BIOSIS
DOCUMENT NUMBER: PREV200300277779
TITLE: The pharmacokinetic properties of posaconazole in fasted healthy subjects: Basis for clinical dosage recommendations.
AUTHOR(S): Ezzet, F. [Reprint Author]; Wexler, D. [Reprint Author]; Courtney, R. [Reprint Author]; Laughlin, M. [Reprint Author]; Batra, V. [Reprint Author]
CORPORATE SOURCE: Schering-Plough Research Institute, Kenilworth, NJ, USA
SOURCE: Abstracts of the Interscience Conference on Antimicrobial Agents and Chemotherapy, (2002) Vol. 42, pp. 20. print.
Meeting Info.: 42nd Interscience Conference on Antimicrobial Agents and Chemotherapy. San Diego, CA, USA. September 27-30, 2002. American Society for Microbiology.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 11 Jun 2003
Last Updated on STN: 11 Jun 2003

AB Background: Posaconazole (POS) is a potent broad-spectrum antifungal agent currently in clinical development for the treatment of invasive fungal infections. The objective of this study was to determine the pharmacokinetics (PK) of POS following the administration of a total POS dose of 800 mg under three different dosage regimens in healthy, fasted volunteers. Methods: Eighteen fasted, healthy volunteers participated in this Phase I, randomized, open-label, 3-way crossover study. Subjects recevied one of three regimens: A single 800 mg dose (Regimen A), two 400 mg doses separated by 12 hr (Regimen B), or four 200 mg doses separated by 6 hr (Regimen C). Plasma POS concentrations were determined from 0-48 hr post-initial dose using a validated HPLC assay. A one compartment oral model with a 1st order rate of absorption and 1st order rate of elimination was fit to the plasma concentration-time data. Differences in exposure were investigated by allowing the bioavailability fraction (F) to vary between regimens. Results: The absorption rate constant was estimated to be 0.2 hr-1, giving an estimated absorption half-life of 3.5 hr. The elimination rate constant was estimated to be 0.045 hr-1, giving an estaimated termination half-life of 15 hr. F was estimated to be significantly different between regimens

(p-value>0.0001). Compared to Regimen A, F for Regimens B and C were estimated to be 1.98 (SE=0.35) and 3.2 (0.7), i.e., an increase in bioavailability of 98% and 220%, respectively. Assuming that the model is predictive upon multiple dosing, steady-state projections would yield AUC (0-24 hr) values of 3900, 7700, and 12400 ng.hr/mL and average concentrations of 162, 320, and 517 ng/mL for Regimens A, B, and C, respectively. Conclusions: Exposure is significantly increased with splitting the 800 mg dose into either 2 (i.e., 2X400 mg) or 4 (i.e., 4X200 mg) doses in fasted, healthy subjects. To enhance exposure under fasted conditions, a split dose regimen is recommended.

L18 ANSWER 14 OF 44 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 2002:555641 BIOSIS
DOCUMENT NUMBER: PREV200200555641
TITLE: Laboratory tools for medical mycology.
AUTHOR(S): Pfaller, M. A. [Reprint author]; Verweij, P. E.
CORPORATE SOURCE: Coll. of Med., Univ. of Iowa, Iowa City, IA, USA
SOURCE: Abstracts of the Interscience Conference on Antimicrobial Agents and Chemotherapy, (2001) Vol. 41, pp. 504. print.
Meeting Info.: 41st Annual Meeting of the Interscience Conference on Antimicrobial Agents and Chemotherapy. Chicago, Illinois, USA. September 22-25, 2001.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 30 Oct 2002
Last Updated on STN: 30 Oct 2002

AB It is apparent that both nosocomial and community-acquired fungal infections are becoming more prominent. This is largely due to an increase in the number of individuals at risk for acquiring fungal infection. As a result, infections due to both common and previously obscure or unusual fungi are being seen more frequently in both the hospital environment and the community. The increase in the frequency and spectrum of fungal infections has coincided with an increase in the number of antifungal agents available for the treatment of infection. In addition to the licensed systemic agents (amphotericin B, fluconazole, itraconazole, ketoconazole and 5-FC), new triazoles with extended spectrums of activity (posaconazole, ravuconazole and voriconazole), novel echinocandin agents (caspofungin, anidulafungin, and micafungin), as well as novel formulations and delivery systems (lipid formulations of amphotericin B and nystatin; intravenous itraconazole) are available or under investigation. Due to the severe and prolonged immunosuppression associated with HIV infection and organ transplantation, it is often necessary to provide long term suppressive therapy to adequately treat fungal infection in these individuals. This situation presents the potential for development of resistance in formerly susceptible strains. It is now apparent that resistance to antifungal agents is an issue of both clinical and epidemiologic importance. All of these factors have combined to increase the need for reproducible, clinically relevant antifungal susceptibility testing for both yeasts and moulds. Antifungal susceptibility (resistance) testing has been standardized and now plays an increasingly important role in guiding therapeutic decision making, as an aid in drug development studies, and as a means of tracking the development of antifungal resistance. In addition to in vitro resistance detection, one of the major strategies to control the spread of infectious diseases and reduce antimicrobial use, and thus resistance, is to develop improved diagnostic strategies. Unfortunately, existing microbiologic methods are slow, insensitive, and are imprecise markers for complete eradication of infection. Although culture independent diagnostic tests for invasive fungal infection are limited, they include detection of antigens and metabolites and the use of nucleic acid-based methods. All of these

approaches offer the potential for rapid detection of fungal pathogens, but currently are limited in availability and usage. Further development of both antifungal susceptibility testing and rapid diagnostic technologies will be important and will require careful clinical and epidemiologic studies for validation. If rapid and sensitive methods for diagnosis, identification and resistance detection can be developed at competitive prices, they will improve diagnosis and therapy and reduce emergence of drug resistance by more appropriate and targeted antimicrobial therapy.

L18 ANSWER 15 OF 44 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 2002:499319 BIOSIS
DOCUMENT NUMBER: PREV200200499319
TITLE: Potential for a drug interaction between Posaconazole and Rifabutin.
AUTHOR(S): Courtney, R. D. [Reprint author]; Statkevich, P. [Reprint author]; Laughlin, M. [Reprint author]; Radwanski, E. [Reprint author]; Lim, J. [Reprint author]; Clement, R. P. [Reprint author]; Batra, V. K. [Reprint author]
CORPORATE SOURCE: Schering-Plough Research Institute, Kenilworth, NJ, USA
SOURCE: Abstracts of the Interscience Conference on Antimicrobial Agents and Chemotherapy, (2001) Vol. 41, pp. 4-5. print.
Meeting Info.: 41st Annual Meeting of the Interscience Conference on Antimicrobial Agents and Chemotherapy. Chicago, Illinois, USA. September 22-25, 2001.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)
LANGUAGE: English
ENTRY DATE: Entered STN: 25 Sep 2002
Last Updated on STN: 25 Sep 2002

AB Background: Posaconazole (POZ) is a broad-spectrum triazole antifungal agent developed to treat a wide variety of invasive fungal infections. POZ inhibits CYP3A4 metabolism, whereas, Rifabutin (RB) is an inducer of CYP3A4. Methods: A non-randomized, open-label, parallel-group, multiple-dose study was conducted to assess the potential for a drug interaction between RB and POZ. Healthy adult male volunteers (n=24) received either of the following two treatments: POZ (200 mg QD) on Days 1 to 10, or RB (300 mg QD) on Day -7 to Day 10 co-administered with POZ (200 mg QD) on Days 1 to 10. Blood samples were collected on Days -1 (RB) and 10 (RB and POZ) for pharmacokinetic (PK) evaluation. Plasma POZ and RB concentration-time data were analyzed by model-independent methods and the PK parameters were statistically evaluated using ANOVA. Changes in the area under the curve within a dosing interval (AUC(tau)) and maximum plasma concentration (Cmax) were evaluated for RB and POZ following co-administration. Results: The mean PK parameters for POZ and RB at steady-state. Conclusion: Clearance of POZ increased 2-fold in the presence of RB while Cmax and AUC(tau) values were reduced by 57 and 51%, respectively. Plasma RB Cmax and AUC(tau) values after co-administration with POZ increased by 31 and 72%, respectively. Therefore, at this time we cannot recommend co-administration of POZ with RB.

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ACCESSION NUMBER: 2002:499318 BIOSIS
DOCUMENT NUMBER: PREV200200499318
TITLE: Potential for a drug interaction between Posaconazole and Phenytoin.
AUTHOR(S): Courtney, R. D. [Reprint author]; Statkevich, P. [Reprint author]; Laughlin, M. [Reprint author]; Pai, S. [Reprint author]; Lim, J. [Reprint author]; Clement, R. P. [Reprint

author]; Batra, V. K. [Reprint author]
CORPORATE SOURCE: Schering-Plough Research Institute, Kenilworth, NJ, USA
SOURCE: Abstracts of the Interscience Conference on Antimicrobial Agents and Chemotherapy, (2001) Vol. 41, pp. 4. print.
Meeting Info.: 41st Annual Meeting of the Interscience Conference on Antimicrobial Agents and Chemotherapy. Chicago, Illinois, USA. September 22-25, 2001.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)
LANGUAGE: English
ENTRY DATE: Entered STN: 25 Sep 2002
Last Updated on STN: 25 Sep 2002

AB Background: Posaconazole (POZ) is a broad-spectrum triazole antifungal agent developed to treat a wide variety of invasive fungal infections. POZ inhibits CYP3A4 metabolism, whereas, Phenytoin (PH) is an inducer of CYP3A4 metabolism. Methods: This randomized, open-label, parallel-group, multiple-dose study with POZ and PH was conducted in healthy male and female adult volunteers (n=36) to assess the potential for a drug interaction between PH and POZ. Each subject was randomized to receive one of the following three treatments: Treatment A: POZ (200 mg QD) for 10 days, Treatment B: PH (200 mg QD) for 10 Days, and Treatment C: POZ (200 mg QD) and PH (200 mg QD) for 10 days. Blood samples were collected on Days 1 and 10 for pharmacokinetic (PK) evaluation of POZ and PH. Plasma data were analyzed by model-independent methods, and PK parameters were evaluated using ANOVA to assess changes in the area under the curve over 24 hr (AUC(0-24hr)), maximum plasma concentration (Cmax) and accumulation ratio (R) between Days 1 and 10 for both POZ and PH. Results: Cmax and AUC(0-24hr) values of POZ on Day 10 when administered alone were approximately 2-fold higher than those on Day 1 (R apprx2); the steady state clearance (CL/F) on Day 10 was 30.3L/hr. In the presence of PH, however, the CL/F increased by apprx90% and the Cmax and AUC(0-24hr) values of POZ on Day 10 were similar to those on Day 1 (R apprx1). Within the limits of variability (%CV ranging from 22-77%), PH Cmax and AUC(0-24 hr) values showed no statistically significant differences (p>0.05) following single and multiple dose administration of PH in the presence or absence of POZ. Conclusion: The large variability in the Cmax and AUC(0-24hr) values was due to some individuals with clinically significant increases in exposure of PH in the presence of POZ. Therefore, at this time we cannot recommend co-administration of POZ with PH.

L18 ANSWER 17 OF 44 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 2002:499317 BIOSIS
DOCUMENT NUMBER: PREV200200499317
TITLE: Effect of Posaconazole on the pharmacokinetics of Cyclosporine.
AUTHOR(S): Courtney, R. D. [Reprint author]; Statkevich, P. [Reprint author]; Laughlin, M. [Reprint author]; Lim, J. [Reprint author]; Clement, R. P. [Reprint author]; Batra, V. K. [Reprint author]
CORPORATE SOURCE: Schering-Plough Research Institute, Kenilworth, NJ, USA
SOURCE: Abstracts of the Interscience Conference on Antimicrobial Agents and Chemotherapy, (2001) Vol. 41, pp. 4. print.
Meeting Info.: 41st Annual Meeting of the Interscience Conference on Antimicrobial Agents and Chemotherapy. Chicago, Illinois, USA. September 22-25, 2001.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)
LANGUAGE: English

ENTRY DATE: Entered STN: 25 Sep 2002
Last Updated on STN: 25 Sep 2002

AB Background: Posaconazole (POZ) is a broad-spectrum triazole antifungal agent developed to treat a wide variety of invasive fungal infections. Cyclosporine (CS) is metabolized by the CYP3A4 metabolic pathway, which is inhibited by POZ. Methods: This open-label, multiple-dose study was conducted to assess the potential for a drug interaction between CS and POZ. Male and female adult heart transplant patients (n=4) maintained on CS upon entering the study, received 200 mg POZ (QD) for 10 days. Blood samples were collected on Days 1 (CS only) and 10 (CS+POZ) for pharmacokinetic analysis. CS safety monitoring was conducted on Days 2, 3, 5, 8, 21 and 28 prior to the morning CS dose. If CS concentrations were elevated dose adjustments were made. POZ and CS concentration-time data were analyzed using model-independent methods. CS maximum plasma concentration (Cmax) and area under the curve values within a dosing interval (AUC(tau)) were dose normalized (DN). Results: Three of the four patients that completed the study required adjustment of their CS dose (14.3-28.6% reduction). The individual steady-state CS clearance values were 16-33% lower on Day 10 vs. Day 1. The DN-Cmax and DN-AUC(tau) values of CS on Day 10 in the presence and absence of POZ differed by only 4.2%. The dosage adjustments were considered low, but indicated that CS concentrations increased when co-administered with POZ. Conclusion: Concomitant administration of CS and POZ led to a 0-29% reduction of CS doses in heart transplant patients. POZ was safe and well tolerated but monitoring of patient CS concentrations for dosage adjustments is recommended when CS is co-administered with POZ.

L18 ANSWER 18 OF 44 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 2001:308511 BIOSIS
DOCUMENT NUMBER: PREV200100308511
TITLE: Use of posaconazole (SCH56592) for treatment of invasive fungal infections refractory to standard antifungal therapy.
AUTHOR(S): Mellinghoff, Ingo [Reprint author]; Mukwaya, Geoffrey; Winston, Drew [Reprint author]; Schiller, Gary [Reprint author]
CORPORATE SOURCE: Hematology/Oncology, School of Medicine, UCLA, Los Angeles, CA, USA
SOURCE: Blood, (November 16, 2000) Vol. 96, No. 11 Part 2, pp. 341b. print.
Meeting Info.: 42nd Annual Meeting of the American Society of Hematology. San Francisco, California, USA. December 01-05, 2000. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 27 Jun 2001
Last Updated on STN: 19 Feb 2002

AB Currently available antifungal agents often fail in immunocompromised hosts. We report 2 patients with hematologic malignancies and invasive mycoses who responded to a new antifungal drug, Posaconazole, after failing standard antifungal therapy. In 1 patient, a 40-year-old man on maintenance chemotherapy for ALL, sinusitis due to Aspergillus niger, Aspergillus flavus, Candida albicans, and Alternaria species developed during prolonged neutropenia. After 3 weeks of oral Itraconazole, fever and worsening headaches led to hospitalization for necrotic sinusitis. Biopsy of sinus tissue revealed septate hyphae and he began therapy with intravenous Amphotericin B. Two weeks later, he developed 2 brain abscesses. The larger abscess was amenable to partial resection and cultures yielded Scedosporium apiospermum (MICs in mcg/ml:

Ampho > 16, Flu = 32, Keto = 1, Itra = 1, SCH56592 = 0.5). Despite 4 weeks of Amphotericin B (total dose 2.5 gm) and 1 week of oral Ketoconazole, clinical deterioration occurred with appearance of new brain lesions. After 1 week of oral Posaconazole alone (200 mg po qid), there was marked clinical improvement. After 6 months of oral Posaconazole alone (400 mg po bid), there has been almost complete radiographic resolution. Currently, the patient functions independently and remains leukemia-free. In the second patient, a 45-year-old man with relapsed non-Hodgkins lymphoma and myelodysplastic syndrome undergoing allogeneic transplantation, a 5X6-cm right upper lobe lung mass developed during prolonged neutropenia. Despite 4 weeks of intravenous Itraconazole and intravenous Amphotericin B (total dose 1.3 gm, then changed to ABLC with total dose of 15.5 gm) for presumed Aspergillosis, he had recurrent fevers and cough. Repeat chest CT scan revealed significant interval enlargement of the lung mass. Biopsy confirmed septate hyphae with no evidence of lymphoma or acid-fast bacteria. Oral Posaconazole alone (200 mg po qid) was started with prompt resolution of fever. After 3 months of oral Posaconazole alone (400 mg po bid), there has been significant radiographic improvement and near-complete resolution of clinical symptoms. In both cases, clinical improvement occurred a few days after initiation of Posaconazole and failure of standard antifungal therapy. Radiographic improvement occurred more slowly. Further clinical studies of Posaconazole for invasive fungal infections are warranted.

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ACCESSION NUMBER: 2001:45188 BIOSIS
DOCUMENT NUMBER: PREV200100045188
TITLE: An open non-comparative multicenter study to evaluate efficacy and safety of Posaconazole (SCH 56592) in the treatment of invasive fungal infections (IFI) refractory (R) to or intolerant (I) to standard therapy (ST).
AUTHOR(S): Hachem, R. Y. [Reprint author]; Raad, I. I. [Reprint author]; Afif, C. M. [Reprint author]; Negroni, R.; Graybill, J.; Hadley, S.; Kantarjian, H. [Reprint author]; Adams, S.; Mukwaya, G.
CORPORATE SOURCE: Univ of Texas M. D. Anderson Cancer Ctr., Houston, TX, USA
SOURCE: Abstracts of the Interscience Conference on Antimicrobial Agents and Chemotherapy, (2000) Vol. 40, pp. 372. print.
Meeting Info.: 40th Interscience Conference on Antimicrobial Agents and Chemotherapy. Toronto, Ontario, Canada. September 17-20, 2000. Interscience Conference on Antimicrobial Agents and Chemotherapy; American Society of Microbiology.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 17 Jan 2001
Last Updated on STN: 12 Feb 2002

L18 ANSWER 20 OF 44 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2003088869 EMBASE
TITLE: Caspofungin.
AUTHOR: Chandrasekar P.H.; Manavathu E.K.
CORPORATE SOURCE: Dr. P.H. Chandrasekar, Wayne State Univ. School of Medicine, Division of Infectious Diseases, Harper Hospital, 4 Brush Center, Detroit, MI 48201, United States
SOURCE: Drugs of Today, (1 Dec 2002) Vol. 38, No. 12, pp. 829-846.
Refs: 92

ISSN: 0025-7656 CODEN: MDACAP
COUNTRY: Spain
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 030 Pharmacology
036 Health Policy, Economics and Management
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 13 Mar 2003
Last Updated on STN: 13 Mar 2003

AB Available systemically effective antifungal agents for the treatment of invasive fungal infections are few. With the increasing recognition of a need for newer antifungal drugs, caspofungin has been introduced as the first member of a new class of compounds called echinocandins. This paper reviews the chemistry and mechanism of action of caspofungin, its activity in vitro and in animal models, and clinical pharmacokinetics, clinical efficacy and safety in patients. .COPYRGT. 2002 Prous Science. All rights reserved.

ACCESSION NUMBER: 2003023666 EMBASE
TITLE: Invasive fungal infections in hematology: New trends.
AUTHOR: Martino R.; Subira M.
CORPORATE SOURCE: R. Martino, Division of Clinical Hematology, Hospital de la Sant Creu i Sant Pau, Av. Sant Antoni Ma Claret 167, 08025 Barcelona, Spain. rmartino@hsp.santpau.es
SOURCE: Annals of Hematology, (2002) Vol. 81, No. 5, pp. 233-243. . Refs: 81
ISSN: 0939-5555 CODEN: ANHEE8
COUNTRY: Germany
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 004 Microbiology
016 Cancer
017 Public Health, Social Medicine and Epidemiology
025 Hematology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 29 Jan 2003
Last Updated on STN: 29 Jan 2003

AB Invasive fungal infections (IFI) are among the most feared complications of patients being treated for a hematological malignancy. Currently, most serious IFI occur in patients with acute leukemia and after allogeneic hematopoietic stem cell transplantation. Although Candida albicans and Aspergillus spp. continue to be the main pathogens, the proportion of patients infected by non-albicans species of Candida and other yeasts and by other filamentous fungi is rising in most institutions. Risk factors for the various IFI differ, and it is thus of utmost importance to realize that not all patients are the same with respect to the risk for developing the various IFI. Recent advances in diagnosis now allow the use of very sensitive imaging techniques with an extremely low negative predictive value. Among the novel microbiologic methods, the galactomannan antigen test is now commercially available for routine use in the diagnosis of aspergillosis, while DNA fungal detection is still experimental. For the first time, clinicians now have a broad range of antifungals to chose from, with special emphasis on amphotericin B preparations, novel broad-spectrum azoles, and the echinocandins. However, the exact place of these agents in treating different IFI will need to be found in the near future.

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ACCESSION NUMBER: 2002332283 EMBASE
TITLE: Antifungal chemotherapy: Advances and perspectives.
AUTHOR: Groll A.H.; Walsh T.J.
CORPORATE SOURCE: Dr. A.H. Groll, Ctr. for Bone Marrow Transplantation, Dept. of Pediatric Haematology, University Medical Center, Domagkstrasse 9a, D-48129 Muenster, Germany. grollan@mednet.uni-muenster.de
SOURCE: Swiss Medical Weekly, (15 Jun 2002) Vol. 132, No. 23-24, pp. 303-311. .
Refs: 103
ISSN: 1424-7860 CODEN: SMWWAI
COUNTRY: Switzerland
DOCUMENT TYPE: Journal; (Short Survey)
FILE SEGMENT: 004 Microbiology
037 Drug Literature Index
038 Adverse Reactions Titles
039 Pharmacy
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 3 Oct 2002
Last Updated on STN: 3 Oct 2002

AB Invasive fungal infections have emerged as important causes of morbidity and mortality in immunocompromised patients. In response to this challenge, the field of antifungal chemotherapy has considerably expanded. Fluconazole and itraconazole, introduced in the late 1980s, were the first durably useful alternatives to amphotericin B deoxycholate. The clinical development of the lipid formulations of amphotericin B, and, more recently, that of novel echinocandin derivatives and improved antifungal triazoles each represent milestones in antifungal drug research that have further amplified our therapeutic options. Major progress has been made in harmonising disease definitions, in defining the paradigms of antifungal intervention, and in designing and implementing clinical trials. Standardised methods for in vitro susceptibility testing of yeasts and filamentous fungi have become available, and pharmacodynamic concepts have entered preclinical and clinical drug development. This article reviews the evolution of therapeutic options over the past decade, advances in chemoprevention and empirical antifungal therapy, progress in early diagnosis and pre-emptive therapy, the promise of the new echinocandins and second generation triazoles, as well as perspectives for combination therapies and adjuvant immunoreconstitution. Invasive fungal infections will remain a frequent and important complication of modern medicine; the current momentum in the field of laboratory and clinical antifungal drug research provides hope for substantial progress in prevention and management of these life-threatening infections in the near future.

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ACCESSION NUMBER: 2002310490 EMBASE
TITLE: Granulocyte colony-stimulating factor and other cytokines in antifungal therapy.
AUTHOR: Roilides E.; Farmaki E.
CORPORATE SOURCE: Dr. E. Roilides, Third Department of Paediatrics, Aristotle University of Thesaloniki, Hippokration Hospital, Konstantinoupoleos 49, GR-546 42 Thessaloniki, Greece. roilides@med.auth.gr
SOURCE: Clinical Microbiology and Infection, (2001) Vol. 7, No. SUPPL. 2, pp. 62-67. .
Refs: 41
ISSN: 1198-743X CODEN: CMINFM
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review

FILE SEGMENT: 004 Microbiology
026 Immunology, Serology and Transplantation
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 13 Sep 2002
Last Updated on STN: 13 Sep 2002

AB Invasive fungal infections (IFIs) have emerged as a serious threat in immunocompromised patients during the last two decades. Host defenses including appropriate cytokine responses and intact phagocytic function are necessary to combat IFIs. Several cytokines have been investigated and developed for preventive and therapeutic use. Among them, granulocyte colony-stimulating factor (G-CSF) has been mostly studied and used for various purposes, the most important being the faster recovery from neutropenia [1]. Other cytokines with potential clinical significance in relation to IFI are granulocyte-macrophage colony-stimulating factor (GM-CSF), interferon-γ (IFN-γ) and macrophage colony-stimulating factor. Supported by a large number of preclinical studies but limited clinical results their potential utility against IFI has been suggested. In this review, certain questions related to this issue are discussed based on data already available and an attempt to consider future research is made.

L18 ANSWER 24 OF 44 EMBASE
ACCESSION NUMBER: 2002297857 EMBASE
TITLE: Antifungals targeted to protein modification: Focus on protein N-myristoyltransferase.
AUTHOR: Georgopapadakou N.H.
CORPORATE SOURCE: N.H. Georgopapadakou, NewBiotics Inc., 4939 Directors Place, San Diego, CA 92121, United States. nafsikag@aol.com
SOURCE: Expert Opinion on Investigational Drugs, (2002) Vol. 11, No. 8, pp. 1117-1125. .
Refs: 86
ISSN: 1354-3784 CODEN: EOIDER
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 004 Microbiology
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 5 Sep 2002
Last Updated on STN: 5 Sep 2002

AB Invasive fungal infections have increased dramatically in recent years to become important causes of morbidity and mortality in hospitalised patients. Currently available antifungal drugs for such infections essentially have three molecular targets: 14α demethylase (azoles), ergosterol (polyenes) and β-1,3-glucan synthase (echinocandins). The first is a fungistatic target vulnerable to resistance development; the second, while a fungicidal target, is not sufficiently different from the host to ensure high selectivity; the third, a fungistatic (Aspergillus) or fungicidal (Candida) target, has limited activity spectrum (gaps: Cryptococcus, emerging fungi) and potential host toxicity that might preclude dose escalation. Drugs aimed at totally new targets are thus needed to increase our chemotherapeutic options and to forestall, alone or in combination chemotherapy, the emergence of drug resistance. Protein N-myristoylation, the cotranslational transfer of the 14-carbon saturated fatty acid myristate from CoA to the amino-terminal glycine of several fungal proteins such as the ADP-ribosylation factor (ARF), presents such an attractive new target.

The reaction, catalysed by myristoyl-CoA:protein N-myristoyl-transferase (NMT), is essential for viability, is biochemically tractable and has proven potential for selectivity. In the past five years, a number of selective inhibitors of the fungal enzyme, some with potent, broad spectrum antifungal activity, have been reported: myristate analogues, myristoylpeptide derivatives, histidine analogues (peptidomimetics), aminobenzothiazoles, quinolones and benzofurans. A major development has been the publication of the crystal structure of Candida albicans and Saccharomyces cerevisiae NMTs, which has allowed virtual docking of inhibitors on the enzyme and refinement of structure-activity relationships of lead compounds.

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ACCESSION NUMBER: 2002297448 EMBASE
TITLE: Fungal infections in liver transplantation: Prophylaxis, surveillance, and treatment.
AUTHOR: Razonable R.R.; Paya C.V.
CORPORATE SOURCE: Dr. C.V. Paya, Division of Infectious Diseases, Mayo Clinic, 200 First Street SW, Rochester, MN 55905, United States. paya@mayo.edu
SOURCE: Current Opinion in Organ Transplantation, (2002) Vol. 7, No. 2, pp. 137-143. .
Refs: 71
ISSN: 1087-2418 CODEN: COOTAB
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
009 Surgery
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
048 Gastroenterology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 5 Sep 2002
Last Updated on STN: 5 Sep 2002

AB Fungal infections are significant causes of morbidity and mortality after liver transplantation. Most of the fungal infections are caused by Candida albicans and less frequently by nonalbicans Candida species, Aspergillus species, and Cryptococcus neoformans. The pathogenesis, time of onset, and frequency of invasive fungal infections is unique for the different fungi and is influenced by defined host factors and level of immunosuppression. The improvements in surgical techniques, the dynamic practice of pharmacologic immunosuppression, the increasing awareness of predisposing risk factors, and the use of a variety of preventive strategies (including antifungal, antibacterial, and antiviral prophylaxis) have modified the epidemiology of fungal infection in patients undergoing liver transplantation. This article reviews the changing spectrum of postliver transplantation mycoses and discusses the current strategies in its surveillance, prevention, and treatment. Additionally, novel diagnostic methods and antifungal agents that may impact the treatment of fungal infection in recipients undergoing liver transplantation are discussed. .COPYRGT. 2002 Lippincott Williams & Wilkins, Inc.

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ACCESSION NUMBER: 2002290242 EMBASE
TITLE: Invasive fungal infections in the neutropenic cancer patient: Current approaches and future strategies.
AUTHOR: Groll A.H.; Walsh T.J.

SOURCE: Infections in Medicine, (2002) Vol. 19, No. 7, pp. 326-334.
Refs: 61
ISSN: 0749-6524 CODEN: INMDEG
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
016 Cancer
026 Immunology, Serology and Transplantation
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 29 Aug 2002
Last Updated on STN: 29 Aug 2002

AB Invasive fungal infections are important causes of morbidity and mortality in cancer patients with prolonged neutropenia following dose-intensive chemotherapy or hematopoietic stem cell transplantation. Recent epidemiologic trends indicate a shift toward infections by Aspergillus species, non-albicans Candida species, and previously uncommon fungal pathogens that have decreased susceptibility to current antifungal agents. In the last decade, much progress has been made in establishing disease definitions and paradigms for antifungal intervention and in the design and conduct of interventional clinical trials. This article reviews current approaches to prevention and treatment of opportunistic fungal infections in neutropenic patients and discusses novel approaches to antifungal chemotherapy and supportive measures.

L18 ANSWER 27 OF 44 EMBASE
ACCESSION NUMBER: 2002227812 EMBASE
TITLE: State-of-the-art review of pulmonary fungal infections.
AUTHOR: Wheat L.J.; Goldman M.; Sarosi G.
CORPORATE SOURCE: Dr. L.J. Wheat, Histoplasmosis Reference Laboratory, 1001 West Tenth Street, Indianapolis, IN 46202, United States. lwheat@iupui.edu
SOURCE: Seminars in Respiratory Infections, (2002) Vol. 17, No. 2, pp. 158-181. .
Refs: 267
ISSN: 0882-0546 CODEN: SRINES
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 004 Microbiology
015 Chest Diseases, Thoracic Surgery and Tuberculosis
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 11 Jul 2002
Last Updated on STN: 11 Jul 2002

AB The endemic mycoses are restricted geographically based on environmental and other factors that favor the growth of these organisms in the soil. Histoplasmosis and blastomycosis mostly afflict patients in the Mississippi and Ohio River Valleys whereas coccidioidomycosis occurs primarily in the dessert southwest United States. Cryptococcosis also may present as pulmonary disease, particularly in persons with cellular immune impairment. These mycoses are increasing in importance as causes for opportunistic disease in immunocompromised patients, especially those with acquired immune deficiency syndrome (AIDS). Aspergillus is a common cause of serious invasive fungal infection in granulocytopenic patients, and may cause lung infection in persons with pre-existing pulmonary diseases or atopy. Infections with less virulent

fungi, such as Trichosporon, Fusarium, Alternaria, Pseudallescheria, and dematiaceous fungi, are being recognized more frequently. The lung is the portal of entry for most of these pathogens, and often is prominently involved in the clinical syndrome. This article focuses on the recognition, diagnosis, and management of these important pulmonary mycoses.

L18 ANSWER 28 OF 44 EMBASE

ACCESSION NUMBER: 2002171484 EMBASE
TITLE: Invasive fungal infections:
Evolving challenges for diagnosis and therapeutics.
AUTHOR: Ellis M.
CORPORATE SOURCE: M. Ellis, Fac. of Medicine and Health Sciences, Tawam Hospital, Al Ain, Abu Dhabi, United Arab Emirates.
ellis@emirates.net.ae
SOURCE: Molecular Immunology, (2002) Vol. 38, No. 12-13, pp. 947-957. .
Refs: 52
ISSN: 0161-5890 CODEN: IMCHAZ
PUBLISHER IDENT.: S 0161-5890(02)00022-6
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
026 Immunology, Serology and Transplantation
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 23 May 2002
Last Updated on STN: 23 May 2002

AB Invasive fungal infections (IFI) parallel the explosive increase in the immunocompromized patient population, and are characterized by diagnostic difficulties and extreme mortality. Candidemia in a tertiary referral hospital in the Middle East confirms the current epidemiologic shift in this common blood stream pathogen towards non-malignancy cases (38%) and antifungal prophylaxis failure (20%), high presentation sepsis scores and attributable mortality (32%). Invasive aspergillosis (IA) is also associated with high mortality. Use of non-invasive computerized tomographic (CT) radiologic scanning linked to early administration of high dose liposomal amphotericin B (LAB) is associated with a reduced mortality of 9.5% compared to historical experience of 28%. Life threatening invasive aspergillosis also occurs in patients who are less obviously immunocompromized. Investigations may reveal subtle immune deficits which could place the patient at some risk for an invasive mycosis. Antifungal treatment used in combination with progenitor cell growth factors and γ-interferon has proved successful in such situations of progressive fungal disease unresponsive to antifungal therapy alone. Pharmacologic remodeling of existing compounds by lipidisation reduces both the toxicity denominator and the efficacy numerator of the therapeutic index when compared to the parent drug. A comparative dose study of liposomal amphotericin B in aspergillosis has demonstrated equi-efficacy, generated debate over the ability of the controlled clinical trial to be capable of assessing antifungal efficacy, and illustrated that recovery from an invasive fungal infection may require maximum tolerated doses and immunomanipulation. Several new antifungal strategies are under clinical investigation. These include reformulating existing antifungals, exploitation of the growing knowledge of virulence factors to synthesize antagonists, immune reconstitution and immunoprotection. An interim analysis of an ongoing placebo controlled study of recombinant interleukin-11 to assess its efficacy in reducing sepsis in leukemia patients through prevention of chemotherapy induced gut epithelial cell apoptosis, has demonstrated a difference in the two study arms in sepsis

rates and preservation of gastrointestinal epithelial cell integrity. The unique and special challenges presented by the dynamic epidemiologics of invasive fungal infections are demanding and attracting considerable responses, in the fields of diagnosis and therapeutics. Current strategies need considerable improvement, yet ongoing collaborative efforts will have a positive impact on our understanding of the fungus-host interaction and ultimately our ability to offer better care for our patients with invasive mycoses. .COPYRGT. 2002 Published by Elsevier Science Ltd.

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ACCESSION NUMBER: 2002022526 EMBASE
TITLE: Cavernous sinus thrombosis caused by zygomycosis after unrelated bone marrow transplantation.
AUTHOR: De Medeiros C.R.; Bleggi-Torres L.F.; Faoro L.N.; Reis-Filho J.S.; Silva L.C.; De Medeiros B.C.; Loddo G.; Pasquini R.
CORPORATE SOURCE: Dr. C.R. De Medeiros, Servico Transplante de Medula Ossea, Hospital de Clinicas, Rua General Carneiro, 181 - 15 andar, Curitiba PR 80060-900, Brazil. medeiros@avaion.sul.com.br
SOURCE: Transplant Infectious Disease, (2001) Vol. 3, No. 4, pp. 231-234. .
Refs: 16
ISSN: 1398-2273 CODEN: TIDSFZ
COUNTRY: Denmark
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
009 Surgery
025 Hematology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 24 Jan 2002
Last Updated on STN: 24 Jan 2002

AB Invasive zygomycosis is a devastating fungal infection occurring as an opportunistic infection after bone marrow transplantation (BMT). Sinusitis can lead to fungal infection in immunosuppressed patients, and cavernous sinus thrombosis, an uncommon condition in immunocompetent patients, typically follows an infection involving the medial third of the face, nose, or paranasal sinuses. Patients undergoing unrelated-donor BMT (UD-BMT) are prone to develop life-threatening infections because of poor recovery of cellular immunity. Despite adequate clinical evaluation and treatment, the prognosis of patients with invasive fungal infections is dismal, especially when intracerebral structures are affected. We describe a case of a patient who underwent an UD-BMT and developed cavernous sinus thrombosis after sinusitis due to zygomycosis. Moreover, he also had disseminated fungal (Zygomycetes and Aspergillus) and viral (cytomegalovirus and adenovirus) infections.

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ACCESSION NUMBER: 2001428774 EMBASE
TITLE: Newer antifungal agents and treatment strategies.
AUTHOR: Hossain M.A.; Reyes G.H.; Ghannoum M.A.
CORPORATE SOURCE: M.A. Hossain, Center for Medical Mycology, Department of Dermatology, Case Western Reserve University, 11100 Euclid Avenue, Cleveland, OH 44106-5028, United States. mag3@po.cwru.edu
SOURCE: Reviews in Medical Microbiology, (2001) Vol. 12, No. SUPPL. 1, pp. S3-S12. .
Refs: 84
ISSN: 0954-139X CODEN: RMEMER

COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 004 Microbiology
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
039 Pharmacy
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 28 Dec 2001
Last Updated on STN: 28 Dec 2001

AB Increased awareness in difficult-to-treat fungal infections has lead to increased efforts directed at antifungal drug discovery. Thus, newer formulations of existing antifungal agents and also novel compounds are being developed. Lipid formulations of amphotericin B have facilitated the management of complicated fungal infections by lowering toxicity. Additionally, a new generation of triazoles has shown a broad spectrum of activity against pathogenic fungi, novel compounds acting on the cell wall or cell membrane have shown promise for their antifungal potential. Recent progress in antifungal drug development, strategies and rational combination of the antifungal agents, immuno-adjuvant and supportive measures have proven advantageous for the treatment of complicated invasive fungal infections in immunocompromised patients. Future research is expected to yield safer, more effective and low-cost therapy and prophylaxis against pathogenic fungi. .COPYRGT. 2001 Lippincott Williams & Wilkins.

L18 ANSWER 31 OF 44 EMBASE
ACCESSION NUMBER: 2001288048 EMBASE
TITLE: Genitourinary fungal infections: A therapeutic conundrum.
AUTHOR: Wise G.J.
CORPORATE SOURCE: G.J. Wise, Division of Urology, Maimonides Medical Center, 48-02 Tenth Avenue, Brooklyn, NY 11219, United States. gwise@maimonidesmed.org
SOURCE: Expert Opinion on Pharmacotherapy, (2001) Vol. 2, No. 8, pp. 1211-1226. .
Refs: 143
ISSN: 1465-6566 CODEN: EOPHF7
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 004 Microbiology
028 Urology and Nephrology
030 Pharmacology
036 Health Policy, Economics and Management
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 30 Aug 2001
Last Updated on STN: 30 Aug 2001

AB Fungi cause 8% of nosocomial infections. This is caused, in part, by the increasing pool of immunocompromised patients. Elderly, transplant and HIV patients, as well as premature infants, have become prime candidates for invasive fungal infections. The widespread use of broad spectrum antibiotics plays a role. Utilisation of appropriate antifungal treatment modalities requires an understanding of the pathogenesis of infection. This is a challenging problem as fungi can cause different clinical manifestations that depend on the type of fungal species and patient response to the infection. Although Candida spp. are the most frequent pathogen, other species such as Aspergilla and Cryptococcus have become major pathogens. Environmental fungi which

include Blastomyces, Coccidioides and Histoplasma have become more aggressive in the vulnerable patient. The genitourinary system can be a source or target of disseminated fungal infection. Diagnosis depends on clinical awareness, utilisation of appropriate diagnostic modalities, imaging modalities and a thorough clinical assessment. The treatment of primary (Blastomyces, Coccidioides, Histoplasma) infection generally requires amphotericin B (AmpB). The opportunistic infections (Aspergilla, Cryptococcus and Candida) may respond to the triazoles although AmpB remains the 'gold standard'. Infections caused by Candida spp. represents the greatest challenge to the clinician. The presence of Candida spp. in the urine may indicate colonisation or infection. Untreated, Candida can remain as a 'saprophyte' or develop ascending infection, sepsis or death. The prophylactic use of fluconazole may in itself result in resistant infection, hence the 'conundrum'.

L18 ANSWER 32 OF 44 EMBASE

ACCESSION NUMBER: 2001278419 EMBASE
TITLE: A clinical perspective for the management of invasive fungal infections: Focus on IDSA guidelines.
AUTHOR: Kontoyiannis D.P.
CORPORATE SOURCE: Dr. D.P. Kontoyiannis, Department of Infection Control, Univ. Texas M.D. Anderson Can. Ctr., Box 402, 1515 Holcombe Boulevard, Houston, TX 77030-4095, United States
SOURCE: Pharmacotherapy, (2001) Vol. 21, No. 8 SUPPL. 2, pp. 175S-187S. .
Refs: 139
ISSN: 0277-0008 CODEN: PHPYDQ
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 004 Microbiology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 23 Aug 2001
Last Updated on STN: 23 Aug 2001

AB Invasive fungal infections, especially candidiasis and aspergillosis, are a major cause of morbidity and mortality. Many controversies surround the management of these infections. A critical overview of the recent Infectious Diseases Society of America practice guidelines is provided, as are comments on both the conundrums and future perspectives in medical mycology.

L18 ANSWER 33 OF 44 EMBASE

ACCESSION NUMBER: 2001278417 EMBASE
TITLE: Antifungal pharmacodynamics: Concentration-effect relationships in vitro and in vivo.
AUTHOR: Groll A.H.; Piscitelli S.C.; Walsh T.J.
CORPORATE SOURCE: Dr. A.H. Groll, Immunocompromised Host Section, National Cancer Institute, Building 10, Bethesda, MD 20892, United States
SOURCE: Pharmacotherapy, (2001) Vol. 21, No. 8 SUPPL. 2, pp. 133S-148S. .
Refs: 134
ISSN: 0277-0008 CODEN: PHPYDQ
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 004 Microbiology
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 23 Aug 2001
Last Updated on STN: 23 Aug 2001

AB The pharmacodynamics of antifungal compounds involve relationships among drug concentrations, time, and antimicrobial effects in vitro and in vivo. Beyond better understanding of a drug's mode of action, characterization of these relationships has important implications for setting susceptibility breakpoints, establishing rational dosing regimens, and facilitating drug development. Important advances have been made in the experimental investigation of pharmacokinetics and pharmacodynamics of antifungal drugs; however, much remains to be learned about specific pathogens and specific sites of infection. Increased incorporation of pharmacokinetic and pharmacodynamic principles in experimental and clinical studies with antifungal agents is an important objective that will benefit the treatment and prophylaxis of life-threatening invasive fungal infections in immunocompromised patients.

L18 ANSWER 34 OF 44 EMBASE

ACCESSION NUMBER: 2001274364 EMBASE
TITLE: Caspofungin: Pharmacology, safety and therapeutic potential in superficial and invasive fungal infections.
AUTHOR: Groll A.H.; Walsh T.J.
CORPORATE SOURCE: Dr. A.H. Groll, Immunocompromised Host Section, Pediatric Oncology Branch, National Cancer Institute, 10 Center Drive, Bethesda, MD 20892, United States. grolla@mail.nih.gov
SOURCE: Expert Opinion on Investigational Drugs, (2001) Vol. 10, No. 8, pp. 1545-1558. .
Refs: 66
ISSN: 1354-3784 CODEN: EOIDER
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
006 Internal Medicine
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
052 Toxicology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 23 Aug 2001
Last Updated on STN: 23 Aug 2001

AB Invasive fungal infections are important causes of morbidity and mortality in hospitalised patients. Current therapy with amphotericin B and antifungal triazoles has overlapping targets and is limited by toxicity and resistance. The echinocandin lipopeptide caspofungin is the first of a new class of antifungal compounds that inhibit the synthesis of 1,3-β-D-glucan. This homopolysaccharide is a major component of the cell wall of many pathogenic fungi and yet is absent in mammalian cells. It provides osmotic stability and is important for cell growth and cell division. In vitro, caspofungin has broad-spectrum anti-fungal activity against Candida and Aspergillus spp. without cross-resistance to existing agents. The compound exerts prolonged post-antifungal effects and fungicidal activity against Candida species and causes severe damage of Aspergillus fumigatus at the sites of hyphal growth. Animal models have demonstrated efficacy against disseminated candidiasis and disseminated and pulmonary aspergillosis, both in normal and in immunocompromised animals. Caspofungin possesses favourable pharmacokinetic properties and is not metabolised through the CYP450 enzyme system. It showed highly promising antifungal efficacy in Phase II and III clinical trials in immunocompromised patients with oesophageal candidiasis. Caspofungin was

effective in patients with invasive aspergillosis intolerant or refractory to standard therapies. Based on its documented antifungal efficacy and an excellent safety profile, caspofungin has been approved recently by the US Food and Drug Administration for the treatment of invasive aspergillosis in patients who are refractory to or intolerant of other therapies (i.e., amphotericin B, lipid formulations of amphotericin B, and/or itraconazole). Phase III clinical trials in patients with candidaemia and in persistently febrile neutropenic patients requiring empirical antifungal therapy are ongoing. This paper reviews the preclinical and clinical pharmacology of caspofungin and its potential role for treatment of invasive and superficial fungal infections in patients.

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ACCESSION NUMBER: 2001274360 EMBASE
TITLE: New developments in chemotherapy for non-invasive fungal infections.
AUTHOR: Hossain M.A.; Ghannoum M.A.
CORPORATE SOURCE: M.A. Ghannoum, Center for Medical Mycology, Department of Dermatology, University Hospitals of Cleveland, 11100 Euclid Avenue, Cleveland, OH 44106-5028, United States. mag3@po.cwru.edu
SOURCE: Expert Opinion on Investigational Drugs, (2001) Vol. 10, No. 8, pp. 1501-1511. .
Refs: 74
ISSN: 1354-3784 CODEN: EOIDER
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 004 Microbiology
006 Internal Medicine
013 Dermatology and Venereology
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 23 Aug 2001
Last Updated on STN: 23 Aug 2001

AB Dermatomycosis and subcutaneous mycosis comprise the non-invasive fungal infections commonly encountered in clinical practice around the world. The limited activity of early topical antifungal agents prompted the development of more effective systemic agents. While griseofulvin has been used for more than four decades, the use of early azoles, such as ketoconazole have resulted in better patient compliance and thus greater success. However, poor response and recurrence in dermatomycosis, as well as toxicity associated with ketoconazole therapy, has led to the search for newer antifungal agents and more effective treatment strategies. Terbinafine, itraconazole and fluconazole have the advantage of non-toxicity and a broad spectrum of activity. An overview of non-invasive fungal infections, antifungal agents in clinical use and recent developments in antifungal therapy is reviewed in this article.

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ACCESSION NUMBER: 2001177472 EMBASE
TITLE: [Treatment of invasive fungal infections: Present and future].
AZ INVAZIV GOMBAINFEKCIOK TERAPIAJA: JELEN ES JOVO".
AUTHOR: Sinko J.
CORPORATE SOURCE: Dr. J. Sinko, Szent Laszlo Korhaz, Budapest/Szent Laszlo Hospital, Gyali ut 5-7, H-1097 Budapest, Hungary
SOURCE: Lege Artis Medicine, (2001) Vol. 11, No. 3, pp. 206-213. .

Refs: 36
ISSN: 0866-4811 CODEN: LAMEFU
COUNTRY: Hungary
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 004 Microbiology
037 Drug Literature Index
LANGUAGE: Hungarian
SUMMARY LANGUAGE: English; Hungarian
ENTRY DATE: Entered STN: 31 May 2001
Last Updated on STN: 31 May 2001

AB In immunocompromised patients morbidity and mortality caused by invasive fungal infections is increasing. It is difficult to establish early diagnosis of mycosis by laboratory tests currently available. Antifungal drugs are often toxic, their spectrum of action is limited and their cost is substantial. In the search for alternative therapeutic modalities, antifungal compounds were synthesised against several targets of the fungal cell. At present, the following drugs have almost completed drug registration procedures: voriconazole, posaconazole and ravuconazole from the new azol group, a candin named caspofungin, and the polyene liposomal nystatin. Nikkomycin Z, sordarins and some other compounds are also seem to be promising. In addition to new antifungal drugs, substantial improvement in the outcome of invasive fungal infections requires extended diagnostic capabilities, as well as a reappraisal of our principles of prophylaxis and treatment.

L18 ANSWER 37 OF 44 EMBASE
ACCESSION NUMBER: 2001097343 EMBASE
TITLE: The exciting future of antifungal therapy.
AUTHOR: Neely M.N.; Ghannoum M.A.
CORPORATE SOURCE: M.A. Ghannoum, Department of Dermatology, Center for Medical Mycology, University Hospitals of Cleveland, 11100 Euclid Avenue, Cleveland, OH 44106, United States. mag3@po.cwru.edu
SOURCE: European Journal of Clinical Microbiology and Infectious Diseases, (2000) Vol. 19, No. 12, pp. 897-914. .
Refs: 208
ISSN: 0934-9723 CODEN: EJCDEU
COUNTRY: Germany
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 004 Microbiology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 17 May 2001
Last Updated on STN: 17 May 2001

AB Invasive fungal infections are becoming more common. Current therapy is generally limited to amphotericin B in its parent and lipid formulations, 5-fluctyosine, fluconazole, and itraconazole. Toxicity, drug-drug interactions, and increasing fungal resistance reduce the usefulness of these drugs, and the need for new therapies is pressing. This article briefly discusses the limitations of antifungal minimum inhibitory testing, and then summarizes new antifungal drugs in development that have been tested in humans. It also addresses novel treatment strategies such as drug combination therapy, pharmacological reformulations to improve the efficacy or reduce the toxicity of current antifungal drugs, immune function augmentation, and vaccine development. All of these strategies, although in their infancy, will enhance the clinician's ability to care for patients with invasive fungal infections.

L18 ANSWER 38 OF 44 EMBASE

ACCESSION NUMBER: 2000428138 EMBASE
TITLE: Fungal infections in patients with neutropenia: Challenges in prophylaxis and treatment.
AUTHOR: Herbrecht R.; Neuville S.; Letscher-Bru V.; Natarajan-Ame S.; Lortholary O.
CORPORATE SOURCE: Dr. R. Herbrecht, Dept. d'Hematologie et d'Oncologie, Hopital de Hautepierre, 67098 Strasbourg, France. raoul.herbrecht@chru-strasbourg.fr
SOURCE: Drugs and Aging, (2000) Vol. 17, No. 5, pp. 339-351. .
Refs: 83
ISSN: 1170-229X CODEN: DRAGE6
COUNTRY: New Zealand
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 020 Gerontology and Geriatrics
036 Health Policy, Economics and Management
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 21 Dec 2000
Last Updated on STN: 21 Dec 2000

AB Fungal infections are a leading cause of mortality in patients with neutropenia. Candidiasis and aspergillosis account for most invasive fungal infections. General prophylactic measures include strict hygiene and environmental measures. Haemopoietic growth factors shorten the duration of neutropenia and thus may reduce the incidence of fungal infections.
Fluconazole is appropriate for antifungal prophylaxis and should be offered to patients with prolonged neutropenia, such as high-risk patients with leukaemia undergoing remission induction or consolidation therapy and high-risk stem cell transplant recipients. Empirical antifungal therapy is mandatory in patients with persistent febrile neutropenia who fail to respond to broad-spectrum antibacterials. Intravenous amphotericin B at a daily dose of 0.6 to 1 mg/kg is preferred whenever aspergillosis cannot be ruled out. Lipid formulations of amphotericin B have demonstrated similar efficacy and are much better tolerated. Fluconazole is the best choice for acute candidiasis in stable patients; amphotericin B should be used in patients with unstable disease. Use of fluconazole is restricted by the existence of resistant strains (Candida krusei and, to a lesser extent, C. glabrata). Amphotericin B still remains the gold standard for invasive aspergillosis. Lipid formulations of amphotericin B are effective in aspergillosis and because they are less nephrotoxic are indicated in patients with poor renal function. Itraconazole is an alternative in patients who have good intestinal function and are able to eat.
Mucormycosis, trichosporonosis, fusariosis and cryptococcosis are less common but require specific management. New antifungal agents, especially new azoles, are under development. Their broad in vitro spectrum and preliminary clinical results are promising.

ACCESSION NUMBER: 2000392586 EMBASE
TITLE: Antifungal pharmacodynamics: Review of the literature and clinical applications.
AUTHOR: Dodds E.S.; Drew R.H.; Perfect J.R.
CORPORATE SOURCE: E.S. Dodds, Duke University Medical Center, Box 3281, Durham, NC 27710, United States
SOURCE: Pharmacotherapy, (2000) Vol. 20, No. 11 I, pp. 1335-1355. .
Refs: 207
ISSN: 0277-0008 CODEN: PHPYDQ
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 004 Microbiology
006 Internal Medicine

030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 13 Dec 2000
Last Updated on STN: 13 Dec 2000

AB Invasive fungal infections are seen with growing frequency, likely due to increases in numbers of patients at risk of infection. Optimal selection and dosing of antifungal agents are important, as these infections are often refractory to available therapy. In contrast to antibacterials, studies examining the pharmacodynamic properties of antifungals and their application in treating invasive disease often are lacking. Agents administered for invasive infections are amphotericin B, flucytosine, and azole antifungals. Several drugs are under investigation, such as posiconazole, voriconazole, and the echinocandins, and preliminary pharmacodynamic data likely will help shape dosing regimens. Clinical trials that investigated dosage and administration, as well as the potential benefits of combination and sequential therapy, are addressed. In addition, antifungal susceptibility and animal models of infection are discussed.

L18 ANSWER 40 OF 44 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 2000157430 EMBASE
TITLE: New drugs and novel targets for treatment of invasive fungal infections in patients with cancer.
AUTHOR: Chiou C.C.; Groll A.H.; Walsh T.J.
CORPORATE SOURCE: Dr. T.J. Walsh, Pediatric Oncology Branch, National Cancer Institute, National Institutes of Health, 10 Center Drive, Bethesda, MD 20892, United States. walsht@pbmac.nci.nih.gov
SOURCE: Oncologist, (2000) Vol. 5, No. 2, pp. 120-135. .
Refs: 150
ISSN: 1083-7159 CODEN: OCOLF6
COUNTRY: United States
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ENTRY DATE: Entered STN: 25 May 2000
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AB Invasive fungal infections have emerged as important causes of morbidity and mortality in profoundly immuno-compromised patients with cancer. Current treatment strategies for these infections are limited by antifungal resistance, toxicity, drug interactions, and expense. In order to overcome these limitations, new antifungal compounds are being developed, which may improve our therapeutic armamentarium for prevention and treatment of invasive mycoses in high-risk patients with neoplastic diseases.

L18 ANSWER 41 OF 44 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 1999289257 EMBASE
TITLE: Current and future antifungal therapy: New targets for antifungal agents.
AUTHOR: Andriole V.T.
CORPORATE SOURCE: V.T. Andriole, Yale University School of Medicine, 333 Cedar Street, New Haven, CT 06518, United States
SOURCE: Journal of Antimicrobial Chemotherapy, (1999) Vol. 44, No. 2, pp. 151-162. .
Refs: 106
ISSN: 0305-7453 CODEN: JACHDX

COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 004 Microbiology
026 Immunology, Serology and Transplantation
029 Clinical Biochemistry
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 3 Sep 1999
Last Updated on STN: 3 Sep 1999

AB Invasive fungal infections are a major problem in immunocompromised patients. The recent expansion of antifungal drug research has occurred because there is a critical need for new antifungal agents to treat these life-threatening invasive infections. The overview of the development of antifungal therapy which is provided herein reflects the increased interest in this very special area of infectious diseases. Although we have newer, less toxic, antifungal agents that are available for clinical use, their clinical efficacy in some invasive fungal infections, such as aspergillosis and fusariosis, is not optimal. Thus, intense efforts in antifungal drug discovery are still needed to develop more promising and effective antifungal agents for use in the clinical arena.

L18 ANSWER 42 OF 44 EMBASE
ACCESSION NUMBER: 1999251785 EMBASE
TITLE: New approaches to antifungal chemotherapy.
AUTHOR: Viviani M.A.; De Marie S.; Graybill J.R.; Yamaguchi H.; Anaissie E.; Caillot D.
CORPORATE SOURCE: M.A. Viviani, Istituto Igiene Medicina Preventiva, Universita degli Studi di Milano, Milano, Italy. viviani@imiucca.csi.unimi.it
SOURCE: Medical Mycology, Supplement, (1998) Vol. 36, No. 1, pp. 194-206. .
Refs: 176
ISSN: 0966-8454 CODEN: MMSUFX
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 004 Microbiology
030 Pharmacology
036 Health Policy, Economics and Management
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 5 Aug 1999
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AB The antifungal agents currently available to treat invasive fungal infections are limited in both number and usefulness. Treatment with the polyene amphotericin B (AmB), and with several azoles, in particular fluconazole and itraconazole, is the mainstay of antifungal chemotherapy. However, the clinical usefulness of these drugs is hampered by drawbacks associated with their safety and/or efficacy. There are two approaches to overcome this situation. One is to discover and develop new antifungal agents or formulations with advantages over and/or complementary to existing drugs. For this purpose, the following three categories of new drugs have been the major targets of study and development:(i) lipid formulations of polyenes, (ii) azoles (including cyclodextrin-complexes), and (iii) nonazole compounds, particularly those of microbial origin (antibiotics).

L18 ANSWER 43 OF 44 EMBASE

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ACCESSION NUMBER: 1999247543 EMBASE
TITLE: Management of invasive fungal infections in oncological patients.
AUTHOR: Hebart H.; Bokemeyer C.; Loffler J.; Schumacher U.; Kanz L.; Einsele H.
CORPORATE SOURCE: Dr. H. Hebart, Abt. 11, Medizinische Klinik, Eberhard-Karls-Universitat Tubingen, Otfried-Muller-Strasse 10, D-72076 Tubingen, Germany
SOURCE: Onkologie, (1999) Vol. 22, No. 3, pp. 192-197. .
Refs: 37
ISSN: 0378-584X CODEN: ONKOD2
COUNTRY: Germany
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 004 Microbiology
016 Cancer
036 Health Policy, Economics and Management
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English; German
ENTRY DATE: Entered STN: 2 Aug 1999
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AB Invasive fungal infections, especially due to Candida and Aspergillus spp., have become a major cause of infection-related mortality in neutropenic cancer patients. Conventional amphotericin B remains the standard drug for antimycotic therapy, however, new antifungal compounds with broad antifungal activity such as lipid formulations of amphotericin B, new azoles, candins, nikkomycin Z, and pradimicin have been developed and are evaluated in preclinical and clinical studies. In this review the most important antifungal compounds are described, and aspects of disease management in neutropenic and nonneutropenic patients are discussed.

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ACCESSION NUMBER: 97250706 EMBASE
DOCUMENT NUMBER: 1997250706
TITLE: Are we making progress in antifungal therapy?.
AUTHOR: Martino P.; Girmenia C.
CORPORATE SOURCE: Dr. P. Martino, Dept. Cellular Biotechnol Hematology, University 'La Sapienza', via Benevento 6, 00161 Rome, Italy
SOURCE: Current Opinion in Oncology, (1997) Vol. 9, No. 4, pp. 314-320. .
Refs: 56
ISSN: 1040-8746 CODEN: CUOOE8
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review .
FILE SEGMENT: 004 Microbiology
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030 Pharmacology
037 Drug Literature Index
039 Pharmacy
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LANGUAGE: English
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AB Contrary to the case with bacterial infections, progress in the diagnosis and treatment of invasive mycoses in cancer patients has been unsatisfactory. Amphotericin B deoxycholate has remained the drug of choice for severe invasive fungal infections for nearly 40 years. However, its infusion-related side effects, as well

as its toxicity, may at times lead to dose reduction or early discontinuation of the treatment. The introduction of the new triazoles, fluconazole and itraconazole, has improved the therapeutic chances against several fungal infections; however, the need for a broad-spectrum drug in empiric antifungal therapy, the emergence of fluconazole-resistant Candida species, and the limitations of itraconazole in terms of speed of action and erratic oral absorption represent important limitations. Recently, laboratory and clinical research has been directed at the develoment of new formulations of older classes of antifungals, the introduction of new classes of antifungals, and the use of immunomodulation associated with antifungal therapy. This paper reviews the more recent advances in the treatment of fungal infections in cancer patients.